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Development of Sheath-Flow Probe Electrospray Ionization Mass Spectrometry and Its Application to Real Time Pesticide Analysis

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Supporting Information

ABSTRACT: For the real time and direct analysis of chemical constituents from living beings and dry sample, sheath-flow probe electrospray ionization mass spectrometry (SF-PESI-MS) has been newly developed. The components from dry or semidry biological tissues can be extracted using the solvent and picked up by the needle for electrospray. This technique was applied to real-time pesticide analysis of living plants. The results have been validated with that of a well-known system, liquid extraction surface analysis mass spectrometry (LESA-MS). It is demonstrated that SF-PESI-MS can produce reasonable ionization efficiency, which is confirmed by LESA-MS.

KEYWORDS: *sheath-flow probe electrospray ionization mass spectrometry, pesticide analysis, real-time*

INTRODUCTION

Normally agricultural chemicals or pesticides are toxic materials and may cause accidental harm if used inappropriately. Barker et al. reported that the ubiquitous nature of pesticides, with frequent use in agriculture and the household, causes the potential harm to nontarget organisms such as wildlife, humans, and pets. Therefore, special attention is required for the rapid and effective detection and identification of these compounds.[1] A recent review has summarized the past few years of active research on the wide application of mass spectrometry analysis of pesticides and their metabolites in food and water matrices for the food and environmental safety issues.[2]

Ambient mass spectrometry has been flourishing in the application of many fields since its first demonstration in 2004 with the development of desorption electrospray ionization mass spectrometry (DESI-MS) by Cooks and co-workers.[3,4] Following the development of DESI-MS, and direct analysis in real time (DART)[5] many novel ionization methods have been reported by several groups by following the same philosophy of ambient mass spectrometry, and they are very well summarized in a recent review by Fernández et al.[6] DESI-MS was implemented on a portable mass spectrometer for in situ detection of active ingredients in plant tissues and agricultural chemicals from a variety of surfaces.[7] DART coupled with high resolution mass spectrometry (Benchtop Orbitrap Exactive) was applied to the screening of pesticides from the surfaces of fruits in open air. The determination of concentrations by DART was about 10 and 100 times below the tolerance levels established by the United States Environmental Protection Agency (US EPA).[8] Liu et al. recently reported a leaf spray mass spectrometry that can be used for the analysis of chemical constituents of intact plant material, including real-time information on sugars, amino acids, fatty acids, lipids, and alkaloids from living plants.[9]

Intriguingly, in 1999 Hong et al. reported that electrospray could be generated not only through capillaries but also on a conductive solid probe from predeposited sample solutions.[10] In 2007, a modified version of ESI was reported from our laboratory, namely, probe electrospray ionization mass spectrometry (PESI-MS) using a solid needle,[11] and the idea of PESI-MS was originated from field desorption (FD) because FD basically utilizes electrospray phenomenon.[12,13] By PESI-MS, high-quality mass spectra could be obtained for protein and peptides, with reasonably less interference signals from high concentration of salts and detergents.[14,15] Because of high reproducibility and ease in handling, PESI has been used for direct biomolecule analysis from biological tissues.[16−20] PESI incorporated with a side vapor sprayer has been applied to direct profiling of phytochemicals in a section of a tulip bulb in different regions, including basal plate, outer and inner rims of scale, flower bud, and foliage leaves.[17] Additionally, high-throughput negative-mode PESI-MS was developed in our laboratory with the assistance of a side vapor supply.[21] We have also reported recently a solid probe-assisted nanoelectrospray ionization (SPA-nanoESI) wherein a solid needle was used for sampling and a nanocapillary was used for the electrospray.[22]

In 2002 Van Berkel et al. reported a simple spot sampling method using a liquid microjunction surface sampling probe/electrospray ionization mass spectrometry (LMJ-SSP/ESI-MS) system.[23] After this development, a fully automated surface

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sampling device coupled with chip-based infusion nanoelectrospray ionization system has been reported by the same group.[24] Liquid extraction surface analysis mass spectrometry (LESA-MS) is a novel surface profiling technique that combines microliquid extraction from a solid surface with nanoelectrospray mass spectrometry.[25] Recently, Raoch et al. also developed a method called nanospray desorption electrospray ionization (Nano-DESI) for liquid-extraction surface sampling in mass spectrometry.[26] These developments inspired us to build up a novel PESI system using sheath liquid flow with a solid probe, namely, sheath-flow probe electrospray ionization mass spectrometry (SF-PESI-MS). This technique could be applicable to the direct analysis of dry samples and biological tissues. In this study, the SF-PESI-MS system is demonstrated for real-time analysis of pesticides from living plant tissues, which is very simple in instrumentation and chiefly applicable to the dry materials that can be made soluble by the electrospray friendly solvents.

EXPERIMENTAL PROCEDURES

SF-PESI-MS. Since the application of PESI-MS was restricted to liquid sample and wet biological tissues, the SF-PESI-MS system was developed for dry samples. For the novel design of SF-PESI, the sample picking-up and spraying process are nearly equivalent to our previous PESI system; notably the sharp solid needle is inserted into the plastic capillary with a protrusion depth of about 0.1−0.2 mm, and solvent is supplied through the tube to the needle tip by a syringe pump. A schematic of the SF-PESI-MS system is shown in Figure 1.

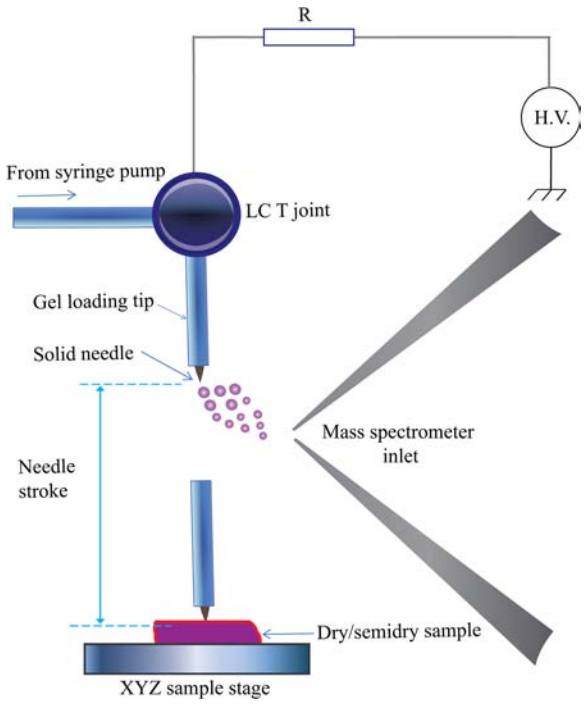

Figure 1. Schematic showing sheath-flow probe electrospray ionization mass spectrometry (SF-PESI-MS).

An acupuncture needle (0.12 mm o.d. with tip diameter of 700 nm; Seirin, Shizuoka, Japan) was inserted into the gel loading pipet tips (GELoader, epT.I.P.S., 20 μL, Eppendorf, Germany) with i.d. of about 0.135 mm and o.d. of 0.2 mm. Acetonitrile/H_2O (1/1) with 0.1% formic acid as a solvent was flowed through the capillary with flow rate of 1 μL/min through the LC T-joint. The measurement was started after the liquid flow was stabilized. The continuous liquid flow also provides an indirect means of needle cleaning for adhered sample during each consecutive sampling and spraying.

The needle was driven along the vertical axis perpendicularly to the apex of the ion sampling orifice with frequency of 1 Hz using a linear actuator (Dyadic Systems co. Ltd., Ishikawa, Japan) with an electronic controller of regulated frequency (ARIOS, Tokyo, Japan). The stroke distance of the needle was set to be 10 mm. The needle was driven with the speed of 350 mm/s. The duration time of the needle in touch with the sample surface for sample extraction was 0.2 s. The high voltage of about 2.5 kV was applied to the needle while it was at the highest position and continuously with the duration of time of about 0.8 s (note, frequency is 1 Hz). The samples were positioned on the *xyz* moving stage. For leaves and stems, the needle position was adjusted to just touch the surface with minimal invasion in the sample surface under the optical microscope observation. The sample stage was moved with the speed 0.1 mm/s or faster.

LESA-MS. The LESA experimental procedures were similar to those described by Eikel et al.[25] In brief, plants materials were placed onto a universal adapter plate and then placed into a LESA-enabled TriVersa NanoMate robot (Advion Inc., Ithaca, NY, USA) without further sample preparation, and the selected areas of plant tissues were analyzed. For standard pesticides, the analyte solution was deposited on the Teflon tape, and it was placed onto the adapter. A conductive pipet tip picked up by a robotic arm moves to an extraction solvent reservoir and sucks the volume required. The tip is then moved in close to the surface location about 1 mm above the surface, and the robot dispenses a defined volume of the solvent. After the extraction, the solvent is sucked from the surface and the robotic system moves the tip to make contact with an electrospray ionization (ESI) chip (Advion Inc., Ithaca, NY, USA)[25] to generate a nanoelectrospray directed to the inlet of the mass spectrometer (LTQ Orbitrap, Thermo Fisher Scientific, Bremen, Germany). A new tip and nozzle were used for every sample to eliminate cross-contamination. The experimental parameters are as follows: 1.2 μL of solvent, dispensing 0.7 μL at maximum speed and wait for 1 s, aspirate 0.9 μL and wait for 1 s, repeat dispensation/aspiration cycle three more times, dispensation height 0.4 mm and aspiration height 0 mm. Nanoelectrospray was initiated with 1.4 kV and a pressure of 0.3 psi in positive ion mode. The extraction/spray solvent used in this study was 50:50 acetonitrile/water, 0.1 vol % formic acid.

Mass Spectrometers. The ions generated by SF-PESI were sampled through the ion-sampling orifice with an inner diameter of 0.4 mm into the vacuum chamber and mass analyzed by an orthogonal time-of-flight mass spectrometer (JEOL, AccuTOF, Akishima, Tokyo, Japan). The temperature of the ion sampling orifice was set at 80 °C. The ions detected by a microchannel plate were converted to digital signals by a 4 GHz time-to-digital converter. The signal integration time of the digital signal averager was adjusted to be 0.5 s. Though the present SF-PESI-MS system was coupled with a TOF mass spectrometer, it could be easily installed to the ion trap, orbitrap, and other mass spectrometers. Exact mass analysis for identification of observed peaks and LESA-MS experiments were performed with a high-resolution mass spectrometer (LTQ Orbitrap) and operated at ultra high resolution mode.

Chemicals and Reagents. All reagents and solvents used in this study were of analytical grade or higher and were used without further purification. Water was purified and deionized by a Milli-Q system (Millipore, Bedford, MA, USA). HPLC grade organic solvents were purchased from Kanto Chemicals (Tokyo, Japan). Agrochemicals (pesticides and fungicides) were purchased from Sumitomo Chemical Garden Products Inc. (Tokyo, Japan) and Sigma-Aldrich (St. Louis, MO, USA).

Pesticides in Plants. *Penetration of Permeable Pesticides into the Plants.* The granular pesticides formulation (Orutoran DX) containing mixture of acephate (2.5%), clothianidin (0.25%), and mineral powders (97.25%) is one of the systemic pesticides in Japan, which is normally applied to the roots of the plants. The jade (*Crassula ovata*) plants grown in the garden of Nissan Chemical Industries Ltd. were transferred to small gardening pots and used as model plants for the experiments. Ten milliliters of aqueous solution containing 1 g of

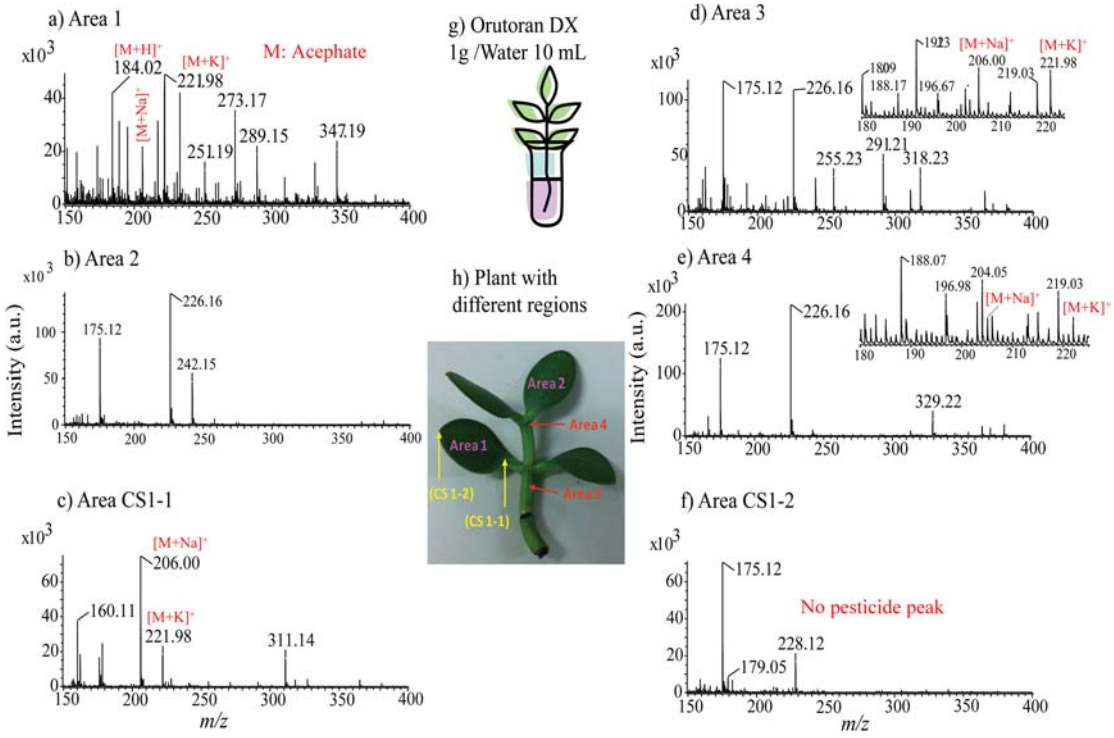

Figure 2. Mass spectra measured by SF-PESI-MS in different regions of a plant for monitoring of the presence of pesticides. (a–f) Mass spectra measured at the different regions: area 1 (a), area 2 (b), area CS1-1 (c), area 3 (d), area4 (e), and area CS1-2 (f), as shown in panel h. (g) Schematic for plant of watering with pesticides. Orutoran DX is the mixture of acephate, chlothianidin, and mineral powders.

Orutoran DX powder was given to the roots of the plants, and they were then kept at 25 °C in a room where sunshine was available in the daytime. After 1 week, the plant samples were subjected to the analysis. The dose used in these experiments (1 g/10 mL) is recommended to gardeners by the manufacturer.

Distribution of Pesticide and Germicide after Spraying. Ivy (*Hedera helix*) and jade (*Crassula ovata*) plants taken from the garden of Nissan Chemical Industries Ltd. were used as the model plants for this experiment. The plants were transferred to small gardening pots and agrochemical (Mospiran Topjin M Sprayer) containing acetamiprid (0.005%), thiophanate-methyl (0.04%), and water with surfactant: 99.955% was sprayed once on the leaf. One half of the leaf was covered by aluminum foil during spraying to ensure that half of the leaf was free from pesticides and germicides. The liquid amount sprayed was about 0.8 mL per leaf. Prior to the LESA-MS and SF-PESI-MS experiments, the plants were kept for a week at 25 °C in a room where sunshine was available in the daytime.

RESULTS AND DISCUSSION

Direct Analysis of Pesticides from Different Parts of Plants by SF-PESI-MS. In modern agriculture, pesticides have been broadly employed in order to protect agricultural products against harmful insects and weeds for improving the quality and increasing the crops yields.[27,28] Acephate belongs to a large group of organophosphorus pesticides, known to be inhibitors of acetylcholinesterase activity, which have been extensively used in world agriculture to control insects from a number of economically significant crops.[29] Clothianidin, a neonicotinoid insecticide, has been found by former Agro Division, Takeda Chemical Industries, Ltd. (Sumitomo Chemical Co., Ltd., at present), and codeveloped with Bayer CropScience.[30] Clothianidin is normally used for seed treatment due to its insecticidal activity for a wide range of economically important plants.[31] However, there must be concerns about hidden harmful impacts of this class of insecticides on nontarget organisms. Principal concerns involve risks to pollinators that may be exposed to chloronicotinyl residues from plant's pollen and nectar.[32] For these reasons, we have used the commercially available agrochemicals under the Japan name Orutoran DX, which is a mixture of acephate (2.5%), clothianidin (0.25%), and mineral powders (97.25%). The mixture of samples was dissolved in water at a concentration of 1 g/10 mL as per the company guidelines. The solution was used to water the *Crassula ovata* plant on the soil. After a week without further watering to the plants, the stem and leaves were used to analyze the distribution of pesticides from lower parts to upper parts. Figure 2(a–f) shows the mass spectra obtained from area 1, area 2, and area CS1-1, area 3, area 4, and area CS1-2, as shown in Figure 2h. The acephate was only detected in area 1, area 3, and area CS1-1. The absolute intensity of acephate is relatively higher in lower parts and lower leaves of the plants. Interestingly no pesticides were detected on the very upper parts of the plants and end part of the leaves. This indicates that the upper parts of the plats have relatively less or no pesticide intake. It might be because plants like to protect themselves against the uptake of foreign materials that are not essential for nutrition in upper parts during growth. This demonstrates the potential capability of SF-PESI-MS in the real-time pesticide analysis in plants from the applied concentration level of pesticides for agriculture. Similar results have been obtained using the LESA-MS system as shown in Figure 3. It is noted that clothianidin was detected neither by LESA-MS nor by SF-PESI-MS. This might be because the concentration of chlothianidin is 10 times lower than that of acephate in the sample solutions. If we compare both results, SF-PESI-MS could produce better ionization efficiency than LESA-MS for this binary pesticide sample from the *Crassula ovata* plant as the needle could penetrate beneath the surfaces.

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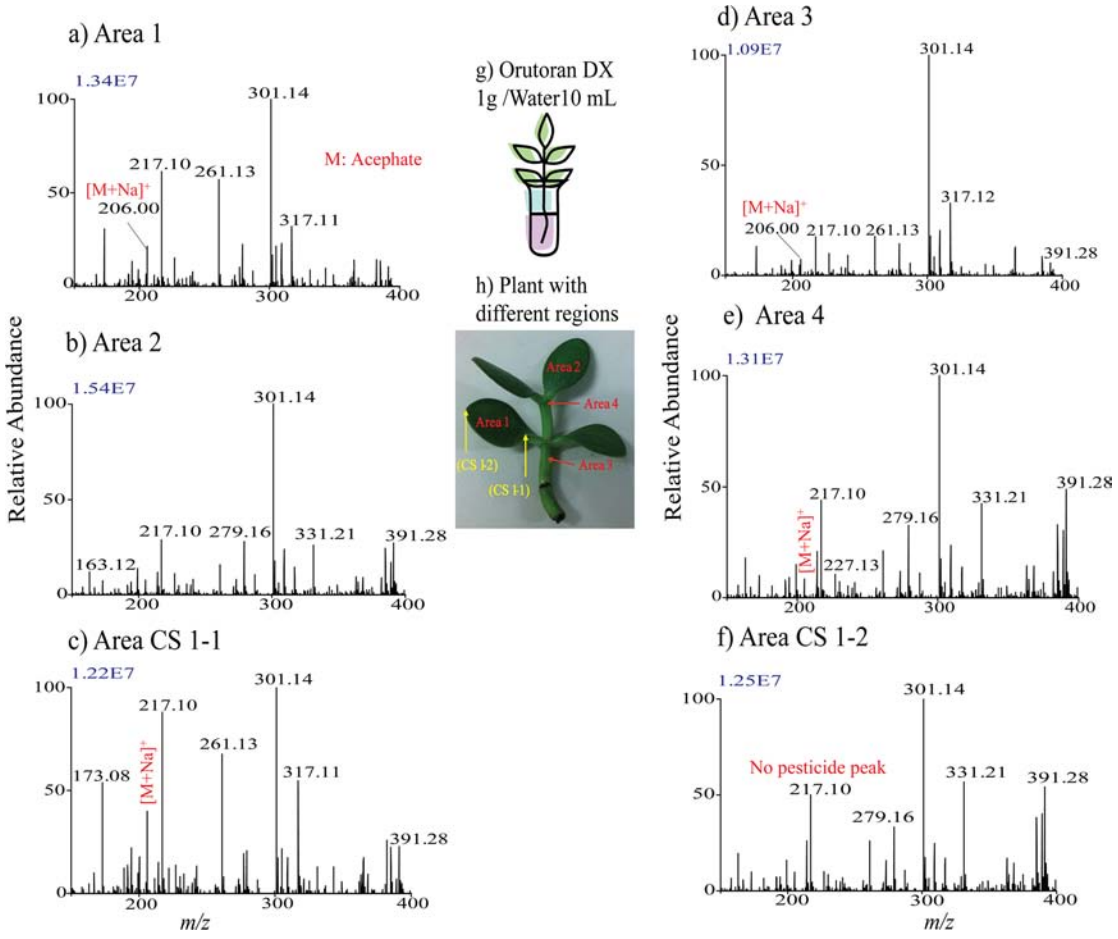

Figure 3. Mass spectra measured by LESA-MS in different region of plant for monitoring of the presence of pesticides. (a-f) Mass spectra measured at the different regions: area 1 (a), area 2 (b), area CS 1-1 (c), area 3 (d), area 4 (e) and area CS 1-2 (f) respectively, as shown in h. (g): Schematic for plant of watering with pesticides. Orutoran DX is the mixture of acephate, chlothianidin, and mineral powders.

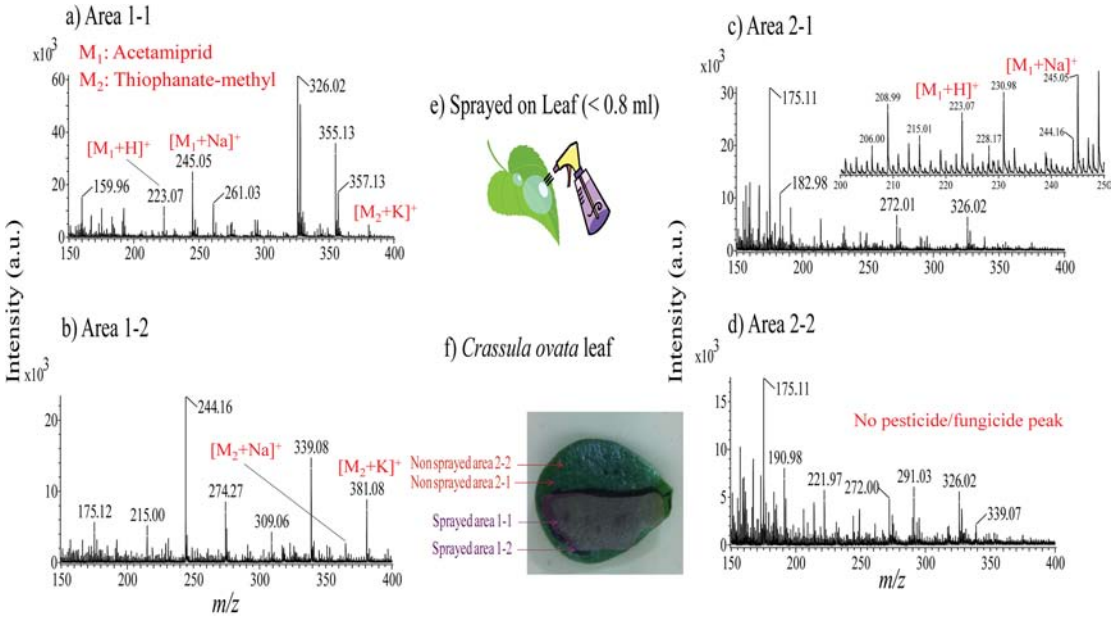

Figure 4. Mass spectra measured by SF-PESI-MS in different regions of *Crassula ovata* leaf for monitoring of the presence of sprayed pesticide and fungicide after a week. (a–d) Mass spectra measured at the different regions: area 1-1 (a), area 1-2 (b), area 2-1 (c), and area 2-2 (d), shown in f. (e): Schematic for the spraying procedures of pesticide and fungicide mixture solution on leaf.

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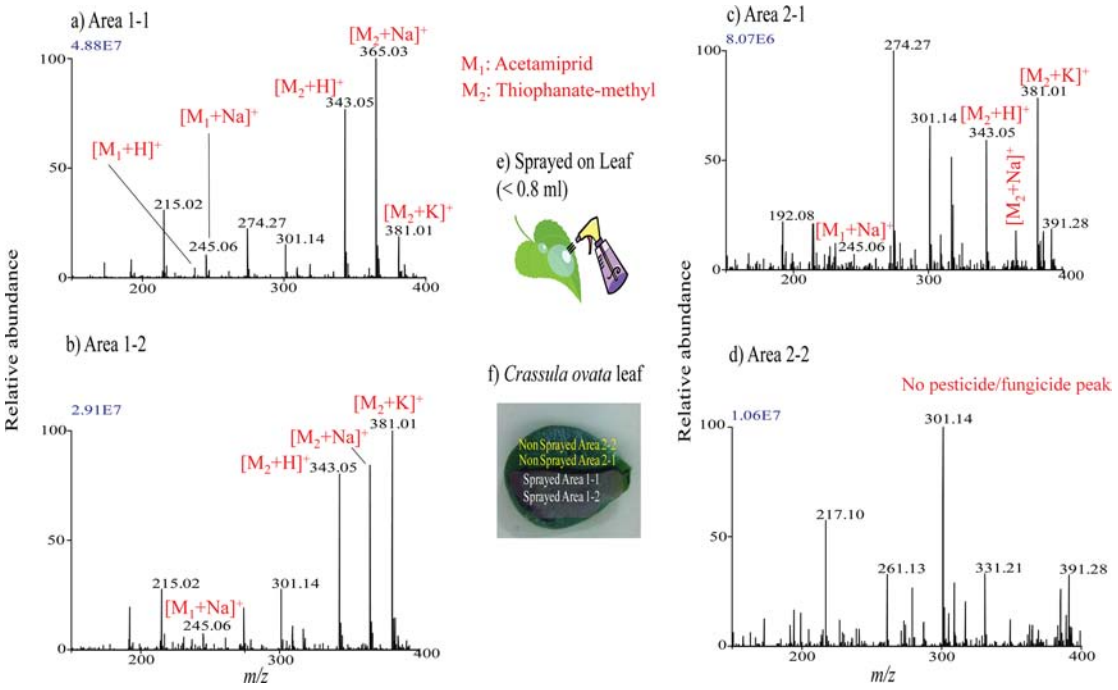

Figure 5. Mass spectra measured by LESA-MS in different regions of *Crassula ovata* leaf for monitoring of the presence of sprayed pesticide and fungicide after a week. (a–d) Mass spectra measured at the different regions: area 1-1 (a), area 1-2 (b), area 2-1(c), and area 2-2 (d), shown in panel f. (e) Schematic for the spraying procedures of pesticide and fungicide mixture solution on leaf.

Direct Analysis of Pesticides from Sprayed Leaf by SF-PESI-MS. The neonicotinoids, which are also called neonicotinyls, chloronicotines, and chloronicotinyls, are a relatively new class of insecticides with a distinct mode of action. Acetamiprid belongs to neonicotinoids and was introduced in Japan during the 1990s.[33] Thiophanate-methyl is widely used as a systemic fungicide for grains, vegetables, and fruit trees.[34] To understand the detection capability of SF-PESI-MS for the analysis of these two agrochemicals, we have used a Mosupiran Topujin M sprayer, which contains acetamiprid (0.005%) and thiophanate-methyl (0.04%) in water with surfactant, 99.955%. Typically a plant leaf has two parts separated by a midrib. The sprayer has been used to spray one side of the midrib of a leaf of *Crassula ovata*, and both sides of the leaf were measured by SF-PESI-MS and LESA-MS after 7 days without further spraying. These experiments were also focused on the observation of agrochemical movement from a sprayed region to a nonsprayed region through the midrib by both methods. A schematic of the spraying system and the mass spectra obtained for all the regions are shown in Figure 4. All the sprayed and nonsprayed regions were divided in two parts (sprayed area 1-1, sprayed area 1-2, nonsprayed area 2-1, nonsprayed 2-2), as shown in Figure 4f. Acetamiprid and thiophanate-methyl were detected by SF-PESI-MS in the sprayed region (Figures 4a,b), and acetamiprid was detected in the nonsprayed are only in the region (marked as 2-1) very close to the sprayed region (Figure 4c). However, SF-PESI-MS completely failed to detect thiophanate-methyl from nonsprayed regions. Similar experiments were performed by LESA-MS, and the results are shown in Figure 5. It is noted that LESA-MS has detected both acetamiprid and thiophanate-methyl peaks from all sprayed regions and the nonsprayed region marked as area 2-1 as shown in Figure 5f; however, no pesticide/fungicide was detected in the region marked as nonsprayed area 2-2 (Fig.5d). It seems likely that no pesticide migrates far from the sprayed region of the plants. To check the reproducibility of the detection capability of these chemicals in different plants, we have applied a similar experimental strategy to the *Hedera helix* plant leaves. The results are similar to those for *Crassula ovata* leaves by SF-PESI-MS and LESA-MS and are summarized in Supplementary Figures 1 and 2 (Supporting Information), respectively. It is not understandable why SF-PESI-MS failed to detect thiophanate-methyl in all the nonsprayed regions. It might be because when sample concentration is low on the surface, LESA-MS gives better ionization efficiency than SF-PESI-MS. Control experiments were performed using the plants materials from *Crassula ovata* and *Hedera helix* plants without applying these agrochemicals by the both SF-PESI-MS and LESA-MS. The results are summarized in Supplementary Figures 3 and 4 (Supporting Information), respectively. These results show that no pesticide has been detected.

In the present study, standard pesticides and fungicide were also used to test the potential quantitative capacity of the SF-PESI-MS technique, even though the main goal of this study is qualitative analysis. One problem faced by the SF-PESI-MS is that the sample loaded to the needle probe cannot be precisely defined during each consecutive measurement and may vary from spot to spot. Therefore, there may be a limitation on the absolute quantitative analysis using SF-PESI-MS.

To examine the quantitative aspect of SF-PESI-MS, the response of intensity versus deposited sample amount was investigated. It is noted that the key step for reproducible results is to move the sample stage at 0.1 mm/s or faster, which could also minimize the cross contamination and sample carry over. If the sample surface is rough, the sampling depth may vary from spot to spot, which may deteriorate the reproducibility. In order to circumvent this problem, a series of experiments using standard acetamiprid in methanol solutions containing from 50 to 3000 pg were made. The sample solutions were spotted on the Teflon tape to examine

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the linear dynamic range of SF-PESI-MS for the detection of dried compounds. Under the experimental conditions, the limit of detection (LOD) was about 50 pg or lower for the standard sample of acetamiprid. However, the absolute amount picked up must be lower than that deposited because the ratio of sample area picked-up by the probe to the area of sample deposited is about 1/30. Supplementary Figure 5a,b (Supporting Information) shows the mass spectra for 50 and 3000 pg of acetamiprid, respectively, deposited on the Teflon tape. Supplementary Figure 5c (Supporting Information) shows analyte concentration versus intensity responses of the peak at m/z 223.07 obtained by using SF-PESI-MS with different concentrations of acetamiprid that can be fitted to $y = 24.18x + 3111$, $R^2 = 0.990$. Similar experiments have been made by LESA-MS using different concentrations of acetamiprid. Under these experimental conditions, the LOD was about 3 pg or lower for the standard acetamiprid sample. Supplementary Figure 6a,b (Supporting Information) shows the mass spectra for 3 and 30000 pg, respectively. Supplementary Figure 6c (Supporting Information) shows analyte concentration versus intensity responses of the peak at m/z 223.07 obtained by using LESA-MS with different concentrations of acetamiprid that can be fitted to $y = 3797x + 2 \times 10^6$, $R^2 = 0.996$. A series of experiments have also been done for three other pesticides for the quantitative analysis using SF-PESI-MS and LESA-MS, and the results are shown in Supplementary Figures 7−12 (Supporting Information). If we compare all quantitative results, LESA-MS is superior to SF-PESI-MS because picked-up liquid volume could be controlled by the LESA-MS, which could give nearly absolute amount of the sample. It is noted that LESA-MS experiments were performed using sampling on the Teflon tape, similar to SF-PESI-MS experiments, just to validate the SF-PESI-MS methodology. The sensitivity achieved from these agrochemicals suggests that SF-PESI-MS may be well applicable to semiquantitative analysis.

Conclusion. In summary, we have demonstrated that pesticides from living plants can be directly ionized and characteristic mass spectra can be obtained under ambient conditions. The experimental setup of this new technique is very simple, and analysis of pesticides from the complex plants materials can be completed within a minute. Although SF-PESI-MS does not provide absolute quantification, our findings with regards to the determination of the distribution of pesticides in different parts of plants and plant leaves may be useful for quality and safety control of foods. We believe that this technique is applicable to food and environmental safety issues as a standard operating procedure. Biological tissue and cell analysis using the present technique is underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

Additional information as mentioned in the text. This information is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions

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Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) Barker, Z.; Venkatchalam, V.; Martin, A. N.; Farquar, G. R.; Frank, M. *Anal. Chim. Acta* **2010**, *661*, 188−194.
(2) Botitsi, H. V.; Garbis, S. D.; Economou, A.; Tsipi, D. F. *Mass Spectrom. Rev.* **2011**, *30*, 907−939.
(3) Takáts, Z.; Wiseman, J. M.; Gologan, B.; Cooks, R. G. *Science* **2004**, *306*, 471−473.
(4) Cooks, R. G.; Ouyang, Z.; Takats, Z.; Wiseman, J. M. *Science* **2006**, *311*, 1566−1570.
(5) Cody, R. B.; Laramée, J. A.; Durst, H. D. *Anal. Chem.* **2005**, *77*, 2297−2302.
(6) Monge, M. E.; Harris, G. A.; Dwivedi, P.; Fernández, F. M. *Chem. Rev.* **2013**, *113*, 2269−2308.
(7) Mulligan, C. C.; Talaty, N.; Cooks, R. G. *Chem. Commun. (Cambridge, U.K.)* **2006**, 1709−1711.
(8) Crawford, E.; Musselman, B. *Anal. Bioanal. Chem.* **2012**, *403*, 2807−2812.
(9) Liu, J.; Wang, H.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2011**, *83*, 7608−7613.
(10) Hong, C.-M.; Lee, C.-T.; Lee, Y.-M.; Kuo, C.-P.; Yuan, C.-H.; Shiea, J. *Rapid Commun. Mass Spectrom.* **1999**, *13*, 21−25.
(11) Hiraoka, K.; Nishidate, K.; Mori, K.; Asakawa, D.; Suzuki, S. *Rapid Commun. Mass Spectrom.* **2007**, *21*, 3139−3144.
(12) Giessmann, U.; Röllgen, F. W. *Int. J. Mass Spectrom. Ion Phys.* **1981**, *38*, 267−279.
(13) Wong, S. S.; Giessmann, U.; Karas, M.; Röllgen, F. W. *Int. J. Mass Spectrom. Ion Processes* **1984**, *56*, 139−150.
(14) Mandal, M. K.; Chen, L. C.; Hashimoto, Y.; Yu, Z.; Hiraoka, K. *Anal. Methods* **2010**, *2*, 1905.
(15) Mandal, M. K.; Chen, L. C.; Yu, Z.; Nonami, H.; Erra-Balsells, R.; Hiraoka, K. *J. Mass Spectrom.* **2011**, *46*, 967−975.
(16) Chen, L. C.; Yoshimura, K.; Yu, Z.; Iwata, R.; Ito, H.; Suzuki, H.; Mori, K.; Ariyada, O.; Takeda, S.; Kubota, T.; Hiraoka, K. *J. Mass Spectrom.* **2009**, *44*, 1469−1477.
(17) Yu, Z.; Chen, L. C.; Suzuki, H.; Ariyada, O.; Erra-Balsells, R.; Nonami, H.; Hiraoka, K. *J. Am. Soc. Mass Spectrom.* **2009**, *20*, 2304−2311.
(18) Yoshimura, K.; Chen, L. C.; Asakawa, D.; Hiraoka, K.; Takeda, S. *J. Mass Spectrom.* **2009**, *44*, 978−985.
(19) Mandal, M. K.; Chen, L. C.; Hiraoka, K. *J. Am. Soc. Mass Spectrom.* **2011**, *22*, 1493−1500.
(20) Mandal, M. K.; Yoshimura, K.; Chen, L. C.; Yu, Z.; Nakazawa, T.; Katoh, R.; Fujii, H.; Takeda, S.; Nonami, H.; Hiraoka, K. *J. Am. Soc. Mass Spectrom.* **2012**, *23*, 2043−2047.
(21) Mandal, M. K.; Saha, S.; Yoshimura, K.; Shida, Y.; Takeda, S.; Nonami, H.; Hiraoka, K. *Analyst* **2013**, *138*, 1682−1688.
(22) Mandal, M. K.; Yoshimura, K.; Saha, S.; Ninomiya, S.; Rahman, M. O.; Yu, Z.; Chen, L. C.; Shida, Y.; Takeda, S.; Nonami, H. *Analyst* **2012**, *137*, 4658−4661.
(23) Van Berkel, G. J.; Sanchez, A. D.; Quirke, J. M. E. *Anal. Chem.* **2002**, *74*, 6216−6223.
(24) Kertesz, V.; Van Berkel, G. J. *J. Mass Spectrom.* **2010**, *45*, 252−260.

(25) Eikel, D.; Vavrek, M.; Smith, S.; Bason, C.; Yeh, S.; Korfmacher, W. A.; Henion, J. D. *Rapid Commun. Mass Spectrom.* **2011**, *25*, 3587−3596.
(26) Roach, P. J.; Laskin, J.; Laskin, A. *Analyst* **2010**, *135*, 2233−2236.
(27) Lee, S. J.; Park, S.; Choi, J. Y.; Shim, J.-H.; Shin, E.-H.; Choi, J.-H.; Kim, S. T.; Abd El-Aty, A. M.; Jin, J. S.; Bae, D. W.; Shin, S. C. *Biomed. Chromatogr.* **2009**, *23*, 719−731.
(28) Park, J.-Y.; Choi, J.-H.; Kim, B.-M.; Park, J.-H.; Cho, S.-K.; Ghafar, M. W.; Abd El-Aty, A. M.; Shim, J.-H. *Biomed. Chromatogr.* **2011**, *25*, 136−146.
(29) Pinjari, A. B.; Novikov, B.; Rezenom, Y. H.; Russell, D. H.; Wales, M. E.; Siddavattam, D. *PLoS One* **2012**, *7*, No. e31963.
(30) Uneme, H. *J. Agric. Food Chem.* **2011**, *59*, 2932−2937.
(31) Ohkawara, Y.; Akayama, A.; Matsuda, K.; Andersch, W. *The BCPC Conference--Pests & Diseases 2002: Proceedings of an international conference*; British Crop Protection Council: Farnham, Surrey, U.K., 2002; pp 51−58.
(32) Cutler, G. C.; Scott-Dupree, C. D. *J. Econ. Entomol.* **2007**, *100*, 765−772.
(33) Obana, H.; Okihashi, M.; Akutsu, K.; Kitagawa, Y.; Hori, S. *J. Agric. Food Chem.* **2002**, *50*, 4464−4467.
(34) Nakamura, M.; Furumi, Y.; Watanabe, F.; Mizukoshi, K.; Taniguchi, M.; Nemoto, S. *J. Food Hyg. Soc. Jpn.* **2011**, *52*, 148−155.