Analytical Methods

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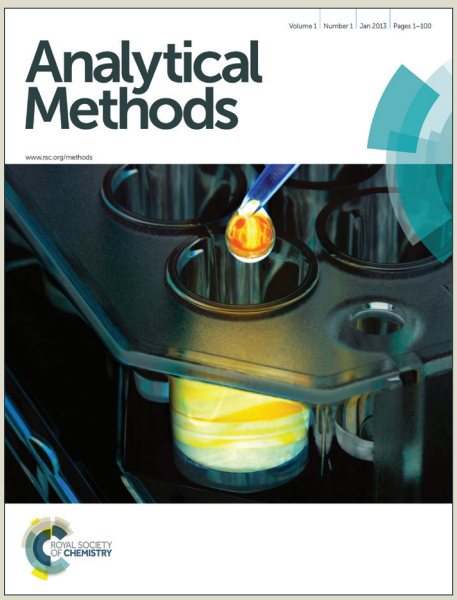

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Analytical Methods

ARTICLE

Direct and fast detection of chlorothalonil in soil samples using laser desorption VUV single photon postionization mass spectrometry

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Wide and abusive applications of fungicides (such as chlorothalonil) in agricultural production have caused various adverse effects on the environment, especially on the soil. Herein, a novel laser desorption VUV single photon postionization mass spectrometry (LDPI-MS) has been firstly applied to the direct and fast detection of chlorothalonil in soil. In the experiment, three different wavelength lasers were used as the ionization sources (SPI at 118 nm, REMPI at 266 nm and 355 nm) and the results showed that only SPI at 118 nm could achieve expected "soft" ionization. The limit of detection in 118 nm ionization was determined to be 0.5 pmol per spot, *ca.* 1 mg/kg of chlorothalonil in soil. Moreover, no other additives were needed to assistant desorption/evaporation of chlorothalonil from soil samples and the detecting process could be rapidly completed on the basis of a time-saving sample pretreatment. The results demonstrated that LDPI-MS method held a great potential for detecting real natural soil contaminated with chlorothalonil.

1.Introduction

Chlorothalonil (2,4,5,6-tetrachloro-1,3-dicyanobenzene) is a typical fungicide and can be effectively against various plant pathogens.[1] However, the excess consumption of chlorothalonil in agriculture has caused serious effects on soil and water, especially on aquatic systems since chlorothalonil is considered highly toxic to fish and invertebrates.[2] In addition, some human diseases including dermatitis, severe eye irritation, and gastrointestinal problems can also be caused by chlorothalonil.[3] Thus, accurate analysis of chlorothalonil in agricultural commodities and soils is crucial for food safety and environmental protection.

Currently, the main technologies for detecting chlorothalonil as well as its degradation products include gas chromatography (GC), liquid chromatography (LC), gas chromatography-mass spectroscopy (GC-MS) and liquid chromatography-mass spectroscopy (LC-MS).[4-6] These methods have shown their advantages in the low detection limit, wide dynamic range and multi-component analysis, but they generally involve extraction, purification and concentration steps, which undoubtedly prolong the detecting time and lead to more complexity of the operation.[7] For example, the entire detection based on GC-MS method is tedious and at least costs over 10 hours for testing.[8-9] To overcome the limitation of time-consuming operation, the enzyme-linked immunosorbent assay (ELISA) approach is developed with the advantages of simplicity and rapidness. However, it requires biological antibody to capture the target which might limit its applications in the routine monitoring of chlorothalonil in the real soil system.[10] Therefore, the development of a simple, efficient and economical method to detect chlorothalonil in real samples still remains a great challenge.

Over the past decade, laser desorption postionization (LDPI) mass spectrometry has proven to be a powerful technique for the direct analysis of target compounds in a variety of matrixes, such as atmospheric aerosols, PAHs-contaminated soil, biomolecules, sediments, asphaltenes, interplanetary dust particles, and meteorities.[11] In 1998, Morrical and his co-worker detected individual organic compound in wood and cigarette smoke particles by LDPI-MS.[12] Luthy et al. detected the PAHs compositions in lamp black-impacted soils nearby the former oil-gas plant in California in 2003.[13] Hanley's group made some contributions to develop this method in the detection of biomolecules such as tryptophan and tyrosine.[14] Dimov detected the quantitative elemental analysis of Rhodium (Rh) and Palladium (Pd) in minerals.[15] Orlando and his co-worker utilized this method to detect organoselenium and organic acid metabolites using laser desorption from graphite surfaces coupled to vacuum ultraviolet single photon ionization mass spectrometry.[16] Additionally, Sabbah and Pomerantz analysed the composition and molecular-mass distribution of asphaltenes.[17-21] Very recently, we used LDPI-MS method with 10.5 eV vacuum ultraviolet single photon ionization (VUV-SPI-MS) to in situ detect medicinal chemicals in tissues dosed in advance.[22] In this assay, the fungicide of chlorothalonil in soil samples is directly analysed for the first time by LDPI-MS

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method, and the detecting process only takes dozens of seconds after a time-saving sample pretreatment.

2.Experimental section

2.1.Principle of LDPI-MS method

LDPI-MS is a flexible technique in which desorption and ionization are separated spatially and temporally with independent lasers. In the desorption step, a pulsed infrared (IR) laser desorbs the target analytes from the surface of sample substrate and results in direct evaporation. The neutral molecule escapes from substrate surface through the rapid laser-induced thermal desorption and forms a gas plume. Previous report reveals that most of the components in the plume are neutral for the pulse energy of the infrared desorption laser (~1.2 eV) is far below the ionization threshold of any potential analytes.[20] Simultaneously, the aggregation is suppressed because of the absence of ion-induced dipole forces.[18,19] In the ionization step, gas-phase molecules in the desorbed plume of neutrals are typically ionized by either VUV single photon ionization (VUV-SPI) or ultraviolet resonant enhanced multiphoton ionization (UV-REMPI).[23] Generally, gas-phase REMPI is considered to be a selective ionization technique via resonant rovibronic transitions, because only molecules with appreciable REMPI cross-sections at the ionization wavelength, such as polycyclic aromatic hydrocarbons (PAHs), are suitable for being ionized.[18] While VUV single photon ionization is a nearly universal ionization method for compounds with ionization energies lower than this photon energy. Previous report reveals that ionization energies for molecules below approximately 400 Da mostly fall between 6 and 12 eV, with the distribution peaking slightly below 9 eV.[24] Therefore, a large fraction of molecular analytes can be ionized by single photon of VUV radiation at 118 nm (*ca.* 10.5 eV).[25]

One of the most significant advantages for LDPI mass spectrometry is that it includes two step processes, allowing laser desorption and laser ionization to be optimized independently.[26,27] It is absolutely different from surface assisted laser desorption ionization (SALDI) mass spectrometry, in which the modified surface of a sample plate assists in transferring energy to the analytes for more efficient desorption and ionization.[28] In comparison with classical technology of matrix-assisted laser desorption/ionization (MALDI) mass spectrometry where the analyte is mixed with a matrix to aid in desorption and ionization, LDPI-MS is simpler and no matrix is needed to add on the substrate to form a good cocrystallization with target molecules.[29,30]

2.2.Apparatus

Time of flight mass spectrometry is a kind of analytical instruments which is based on different *m/z* value of the ions.[31,32] In a time of flight (TOF) mass spectrometer, ions formed in an ion source are extracted and accelerated to a high velocity by an electric field into an analyser consisting of a long straight 'drift tube'. The ions pass along the tube until they reach a detector. After the initial acceleration phase, the velocity reached by an ion is inversely proportional to its mass (strictly, inversely proportional to the square root of its *m/z* value). Since the distance from the ion origin to the detector is fixed, the time taken for an ion to traverse the analyser in a straight line is inversely proportional to its velocity and hence proportional to its mass. Thus, each *m/z* value has its characteristic time-of-flight from the source to the detector.

As shown in Fig. 1, the home-built apparatus for LDPI-MS in our laboratory consists of a high vacuum (HV) chamber (background pressure of 10^{-7}-10^{-8} Torr) equipped with a linear transfer antechamber, a sample holder with an XYZ controller mounted on a rotation stage, a third harmonic generation (THG) cell, and a custom-designed linear time of flight mass spectrometer. (Schematic diagram of the LDPI-MS instrument see in Supplementary Fig. S1). Although it is capable of operating in both linear and reflectron modes, we used the instrument in linear mode for more simply operating and the maximum mass resolution of our home-built LDPI-MS instrument can reach to *ca.* 500. The sample deposited on the substrate was loaded into the antechamber and then transferred to the ionization region by a rotary-linear mechanical transporter after the antechamber pressure was reduced to 10^{-5} Torr.[33]

A 1064 nm Nd:YAG laser (MQU-200-Ⅱ, Zklaser, Beijing) with 10 Hz operational repetition rate was focused on an approximately 0.2 mm^2 spot for desorption. The pulse energy was controlled in the range of 1.0-3.0 mJ/pulse which corresponding to laser fluences of approximately 20-60 MW/cm^2, while the laser was vertically focused on the sample surface from a quartz window at the top of the chamber after being reflected by a prism. The vacuum ultraviolet photons (VUV 118 nm, 10.5 eV) were generated by frequency tripling another Nd:YAG 355 nm laser (INDI-40-10YAG, Spectra-Physics, U.S.A) using a THG cell filled with high-purity mixed gas of xenon and argon. The intensity of 118 nm photon was optimized through increasing the 355 nm laser power and adjusting the gas pressure as well as mixture ratio. In this work, the 10 Hz, 355 nm laser (~40 mJ) was focused on the THG cell by a quartz lens (*f*=35 cm), and the pressure was adjusted to ~200 Torr in phase-matched 1:10 Xe/Ar gas mixtures.[34] The VUV photons were separated from the 355 nm laser through an MgF_2 lens, which had completely different refractive indices for 355 nm beam at the YAG third harmonic (n=1.39) and 118 nm beam at the YAG ninth harmonic (n=1.67).[35,36] The VUV pulse energy was not measured but was estimated to be 0.1 μJ on the basis of an approximate conversion efficiency of 10^{-6}-10^{-5} reported in the literature.[37,38]

In the experiment, the UV/VUV beam horizontally passed through the desorption plume at a distance ~1-2 mm from the sample surface, in parallel to the substrate. The optimized delay time between the desorption laser (1064 nm) and ionization beam was confirmed to be 15-18 μs on the basis of the previous experiment.[22] Herein, the ion signals were detected by MCP detector. The output of the ion signals was digitized, averaged, and recorded by a digital storage oscilloscope (DSO-5032A Agilent Technologies) and stored in a USB flash drive. All time

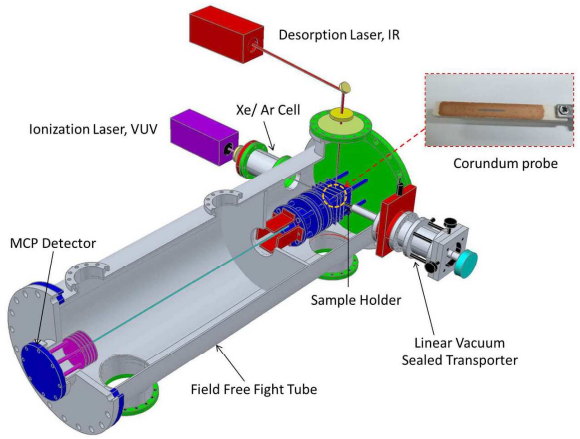

Fig. 1 Three dimensional schematic diagram of the home-built LDPI-MS apparatus.

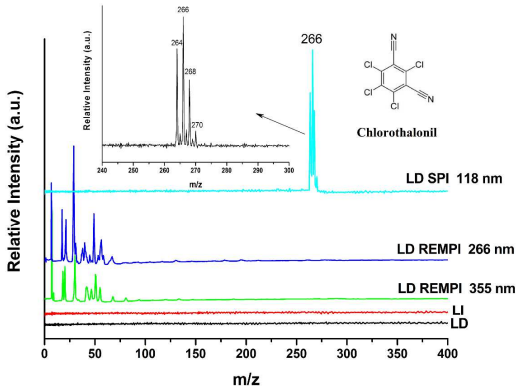

Fig. 2 Mass spectra of chlorothalonil at photon energies of 10.5 eV measured by laser desorption post-ionization (LD SPI 118 nm), only laser ionization (LI), only laser desorption (LD) and in LDPI with different ionization lasers (SPI at 118 nm, REMPI at 266 nm and REMPI at 355 nm, respectively). The inset shows the multiple peaks around *m/z* 266.

coordination was controlled by a digital delay generator (Model DG 535, Stanford Research Systems, Sunnyvale CA).

2.3.Chemicals and soil samples preparation

All chemicals were of analytical regent grade. Chlorothalonil (98%) was purchased from Xiya Reagent Company (Chengdu, China) and directly used without further treatment. Acetone (>99.5%) was obtained from Guangzhou chemical reagent factory. Ultrapure water used in the experiment was deionized and further purified with Elga water purification system (Elga lab water, England). Different concentrations of chlorothalonil standard solutions were prepared by diluting saturated solution with acetone.

As shown in Supplementary Fig. S2, the fresh soil samples used and handled in this work were collected from the farmland in suburb of Guangzhou City and the average sampling depth is *ca.* 10 centimetres under the topsoil. Wet soil was naturally air dried in fuming hood at the laboratory temperature, and then was sifted through a 100 μm metallic screen cloth and reserved in beakers for further experiment. In our experiment, 5 mL of chlorothalonil was added to each prepared soil sample (*ca.* 5 g) in the wild-mouth bottles with different concentrations of 1, 2, 5, 10, 100 mg/L, respectively. To mimic agricultural conditions as closely as possible, the mixtures were firstly shaken in a container for 10 min and then were oscillated for 20 min using a sonicator, finally stored in the dark place.[1] In the present work, we choose corundum rods as the sample substrate. The analytes were directly deposited on the corundum substrate, which were washed in de-ionized water for 1 hour and then cleaned ultrasonically in absolute ethyl alcohol for 30 minutes. The net weight of the deposited soil for each sample probe was controlled to be *ca.* 200 mg and the target area is 3 cm^2 to make sure the soil well spread.

3.Results and discussion

3.1.Analysis of neat chlorothalonil using LDPI-MS

Fig. 2 shows the LDPI-MS of neat chlorothalonil, which is coated on the corundum substrate. It can be seen that no distinct mass spectrum signal is observed when only laser desorption or laser ionization is employed for chlorothalonil (Fig. 2, LD and LI), which indicates that single desorption laser or ionization laser is unable to generate a meaningful signal contribution in this experiment. However, the characteristic peaks related to chlorothalonil appear around *m/z* 266 in mass spectrum when two lasers are simultaneously employed (Fig. 2, LD SPI 118 nm). The inserted spectrum in Fig. 2 displays the amplifying peaks of chlorothalonil cations in the mass spectral area from *m/z* 240 to 300. The features consist of multiply mass spectrum peaks from 264 to 270. Note that the chlorine isotopes ^{35}Cl and ^{37}Cl exist in natural at abundant ratio of 3:1, the peak at *m/z* 266 is the most intense one in the mass spectrum. The results also show that the obtained LDPI mass spectrum is faint except the signal from chlorothalonil, where only several aggregates or fragments ions are detected with the mass weight below 400 Da. Comparing with other photoionization methods, these results indicated that LDPI-MS is a more appropriate method for the detection of chlorothalonil.[39-40] In the following experiments, the parent ion *m/z* 266 ($[C_8C_{14}N_2]^+$) of chlorothalonil is taken as the characteristic signal.

3.2.Superiority of VUV single photon ionization for chlorothalonil detection

For the purpose of verifying which one is most suitable for the soft ionization of fungicide molecules, the mass spectrum for chlorothalonil was also acquired with different ionization techniques such as SPI at 118 nm, REMPI at 266 nm or 355 nm. It is clear shown in Figure 2 that large amounts of fragment ions below *m/z* 100 in REMPI mass spectra are observed. The signals of fragment ions in REMPI mass spectra are chaotic and complicated; which makes it difficult to discriminate the signal of chlorothalonil from the other background features in mass spectra. The details of ionization and chemistry mechanism are

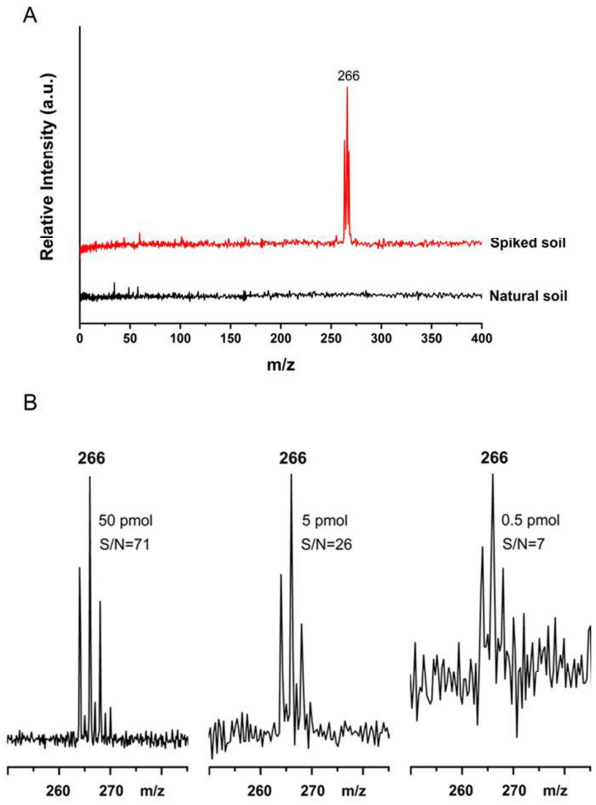

Fig. 3 (A) LDPI-MS analysis of the soil spiked with 0.01 M chlorothalonil and the real natural soil, respectively. **(B)** The limit of detection tested with chlorothalonil-doped soil samples. The S/N was calculated based on the analysis of mass spectra.

not very clear. One of possible reasons is that multiphoton could be absorbed in REMPI, which leads to the total absorbed energies being larger than the ionization potential of chlorothalonil.[23] However, the mass spectrum signal of chlorothalonil parent ion at *m/z* 266 ($[C_8C_{l4}N_2]^+$) appears when single photon ionization at 118 nm acts as ionization laser (as shown in Fig. 2). That implies SPI technique can achieve expected soft ionization under favorable conditions. Apparently, it can be explained by the fact that the chlorothalonil ionization energy (9.25 eV, predicted by ab initio calculations) is approximately close to the single photon energy of 118 nm. Previously, single photon ionization has been approved as a soft ionization source.[41-43] The results confirm that chlorothalonil can be "soft" ionized under 118 nm radiation.

The above results obviously demonstrate that both SPI (118 nm) and REMPI (266 nm and 355 nm) have the capability to ionize chlorothalonil, but only 118 nm SPI realizes the soft ionization. Therefore, 118 nm SPI would be a preferred ionization source in the present analysis approach.

3.3.Detection of chlorothalonil in real soil samples

However, whether LDPI can produce any enough significant mass signals from the neat soil samples is still unknown, especially in the mass range of chlorothalonil. Fig. 3A displays the mass spectrum of the blank soil samples. Only few sporadic, poorly reproducible peaks below *m/z* 150 are observed, which may be related to some organic natural humus residue in soil samples. Fig. 3A also illustrates the LDPI mass spectrum of the soil sample which is spiked with standard solution of chlorothalonil. The signals of the molecular ion $[C_8C_{l4}N_2]^+$ are found to be away from the background signals of soil (*<m/z* 150), which indicates that there is almost no matrix interference in the experiments. The results further validated the feasibility of our approach for direct and fast detection of chlorothalonil in soil samples. The detection of the real contaminated soil would be the next work undertaking in our group.

Notably, no special procedures are used for the blank and spiked soils except for adding some ultrapure water to enhance the adhesion. In addition, it takes 10 minutes in fume cupboard to dry soil samples at the lab temperature. The experiment shows that too fast drying will cause the coated soil fracturing and peeling from the corundum substrate, which is a potential risk in vacuum chamber. Although these programs need to be done in advance, the detecting process will be completed in dozens of seconds.

3.4.Semi-quantification and estimation of the Limit of detection

It is of great importance to drive the detection sensitivity toward the trace level for analysing chlorothalonil in soil samples. There are many factors that impact on the limit of detection such as desorption/evaporation or ionization efficiency, delay time between the two lasers, distance of sample substrate from the ionization laser.[22] For the sake of getting higher detection sensitivity, all the parameters have been optimized. Furthermore, the optimized lasers desorption and ionization conditions were controlled and kept constant during the whole measurements.

Our experiments show that the ion signals using VUV (10.5 eV) photoionization is relatively invariant for the chlorothalonil desorbates in soil sample (see supplementary Fig. S3, Supporting Information). Therefore, quantitative measurements can be achieved by LDPI-MS in present experiments. Fig. 3B showed the amplified mass spectrum of soil samples which were spiked with different mass concentrations of chlorothalonil at 100 mg/kg (50 pmol/spot), 10 mg/kg (5 pmol) and 1 mg/kg (0.5 pmol), respectively (more information see in Supplementary Fig. S4). Here the amount of each analyte deposited on the substrate per spot was calculated using the molecular densities (total amount of analytes divided by sample plate area) multiplied by the spot size of the desorption laser.[16] In order to make the results as accurate as possible, we measured the signal intensities of at least three points located on the different places of the sample surface for each concentration. The data displayed in Fig. 3B as well as Fig. S4 are the average values. The resulting signal-to-noise

ratios acquired from *ca.* 200 mg soil samples are also collectively illustrated. It is clearly indicated that a quantitative limit of detection (QLOD) could reach 0.5 pmol/spot (with the mass concentrations at *ca.* 1 mg/kg) at S/N = 7, which has reached the Chinese standard on the maximum residue limits of chlorothalonil for most vegetables and fruit.[44,45] This limit of detection (LOD) with the LDPI-MS method has reached the level of pmol, which it is about 20-1000 times higher than that with LC/MS method (typically 1-50 ug/kg).[5] Although the detection sensitivity is not very ideal, note that the complicated sample pretreatment is not necessary in the proposed method.[46-48] The lower LOD is expected to be acquired by improving the efficiency of desorption and ionization or optimizing signal acquisition.

In order to obtain the theoretical detection limit, we further obtained the fitting equation about the signal intensity (*m/z* 266) and the amount of chlorothalonil deposited on each soil sample spot in logarithmic scales over the range of 0.5 pmol and 50 pmol using OriginPro software (see supplementary Fig. S5, Supporting Information). Each value comes from the average of at least three spots. The regression equation is Log10Y=-0.33+0.53Log10X with a correlation coefficient of 0.9905, where Y and X are signal intensity of *m/z* 266 and the amount of chlorothalonil deposited on each soil sample spot, respectively. Furthermore, we calculated the theoretical detection limit by evaluating the average signal of blank plus three times standard deviation on the basis of the 3σ method.[49] And the calculated LOD (S/N=3) of chlorothalonil in soil samples is estimated to be about 150 fmol per spot (namely *ca.* 40 pg/spot, with the mass concentration at *ca.* 0.3 mg/kg) by LDPI-MS. The result shows the proposed method has great potential for the semi-quantitative and direct analysis of chlorothalonil in soil samples.

4.Conclusions

In summary, a method for direct and fast detection of chlorothalonil using laser desorption from soil samples deposited on corundum substrate coupled to VUV LDPI-MS is described. Herein, we firstly confirmed the feasibility for the trace chlorothalonil detection in the soil by the use of laser desorption VUV single photon postionization mass spectrometry (LDPI-MS). It is found that the mass spectrum of chlorothalonil by LDPI-MS is very faint except for the parent ion and limited fragments. By comparing the single photon ionization at 118 nm and REMPI at 266 nm as well as 355 nm for chlorothalonil in LDPI-MS, it is verified that only SPI at 118 nm can achieve soft ionization and its parent ion *m/z* 266 ($[C_8C_{l4}N_2]^+$) can be observed. In addition, a series of experiments were accomplished and a quantitative limit of detection of chlorothalonil in real soil samples was determined to be 0.5 pmol per spot (*ca.*1 mg/kg). Theoretical estimated results revealed that femtomolar amounts (150 fmol per spot) of chlorothalonil could be available for analysis. Moreover, no additives are required for the target analytes. The sample pretreatment is time-saving and the detecting process can be completed in dozens of seconds by LDPI-MS method. The improvements of laser desorption efficiency and detector sensitivity will be engaged in our future study.

Acknowledgments

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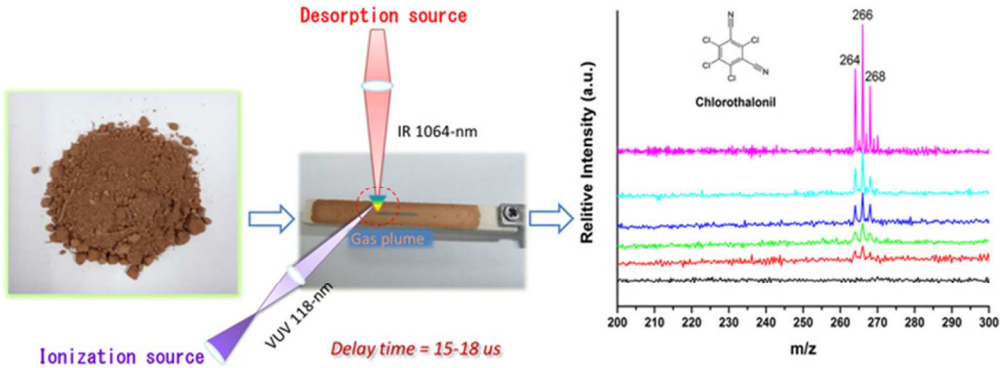

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