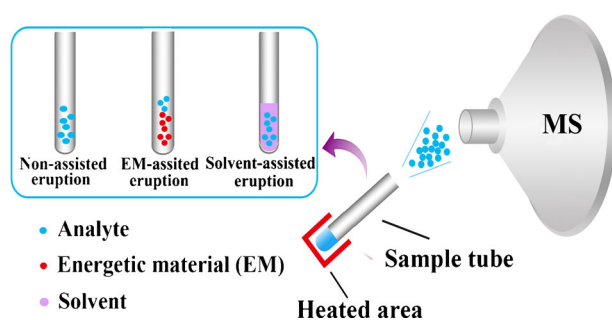


Fast Eruption Desorption Ionization for Mass Spectrometric Analysis

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Abstract. Fast eruption desorption ionization (FEDI) technique was developed for simple, rapid, and sensitive analysis of various compounds. The FEDI allows three analytical modes each with the unique characteristic. The results demonstrated that non-assisted eruption was suitable for stable and volatile compounds, energetic material (EM)-assisted for nonvolatile molecules especially metal compounds, and solvent-assisted eruption for fragile molecules. High-quality mass

spectra with intact ions of analytes were obtained in positive and negative ion modes.

Keywords: Mass spectrometry, Fast eruption desorption ionization, Non-assisted eruption, EM-assisted eruption, Solvent-assisted eruption

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Introduction

Mass spectrometry (MS) is a powerful analytical technique for reasons of high speed, high sensitivity, and the capacity of structure information. The innovation of ion source has been promoting the rapid development of MS [1–3]. Ionization techniques requiring no high voltage or laser have aroused increasing concern with varying degrees of success, such as inlet ionization [4, 5], zero volt paper spray ionization (zvPSI) [6], ambient flame ionization (AFI) [7], atmospheric-pressure thermal desorption ionization (APTDI) [8], etc. These ionization techniques offer great flexibility in MS analysis, which avoids discharge and unwanted redox reactions from the high voltage as well as low mass interference from the matrix. Inlet ionization allows analysis of various compounds, such as carbohydrates, proteins, lipids, synthetic polymers, etc., where the initial ionization happens in the MS inlet. Although this method avoids ion losses from atmospheric pressure to vacuum, the subatmosphere operation condition is restricted

relative to sample introduction and may cause contamination to the mass spectrometer. APTDI generates ions by rapidly heating analytes with the assistance of nitrogen at atmospheric pressure, which is generally used to analyze solid compounds, especially organic salts. Therefore, further investigation is required to develop simple and rapid ionization methods with good compatibility to various samples for growing applications.

It is known that charged droplets and solid particles are pervasive in natural phenomena such as thunderstorm, volcanoes, and waterfall [9–11]. These charged species are mainly generated in the process of high-velocity and violent motion, which inspired us to explore innovative ionization technique given that the charge formation of the analyte is the prerequisite for the MS detection. Here, a fast eruption desorption ionization (FEDI) technique was reported, which was a reflection of macroscopic natural phenomena and generated ions in the process of violent and high-speed eruption in a small space.

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Material and Methods

FEDI-MS Conditions

The FEDI device consists of the sample tube and heating source. The sample tube is the glass tube originating from the method of

direct insertion probe of electron ionization (EI). The disposable glass tube avoids the problems of cross contamination and memory effects. The photograph of FEDI-MS apparatus was shown in Fig. 1. The sample was introduced into the bottom of the sample tube. Then the sample tube held in place by alligator clip was placed in front of the MS inlet. The heating source yielded sufficient energy at the bottom of the sample tube, which rendered the volume of sample rapidly expand. Then the desorption and ionization occurred when the sample in the narrow space was erupted to the atmosphere, accompanied by strong friction and collision. Three different working modes of FEDI-MS analysis were applied including non-assisted eruption, energetic material (EM)-assisted eruption, and solvent-assisted eruption. The details of various experimental parameters were presented in the [Supporting Information](#).

The FEDI-MS and MS/MS experiments were performed on TSQ triple-quadrupole mass spectrometer (Thermo-Fisher Scientific, Waltham, MA, USA). The exact mass measurements were carried out by using a linear ion trap-Fourier transform ion cyclotron resonance mass spectrometer (LTQ-FTICR MS, Thermo-Fisher Scientific, Bremen, Germany).

Detailed information about the chemicals and instruments was listed in the [Supporting Information](#).

Results and Discussion

The experiments were performed to demonstrate the capacity and scope of application of FEDI-MS by analyzing various compounds with different polarities (e.g., PAHs, glycosides, organometallic compounds, etc.). First, analytes were directly introduced into the sample tube, namely non-assisted eruption mode. Then the flame was exposed to the bottom of the sample tube. The analyte rapidly erupted from the sample tube,

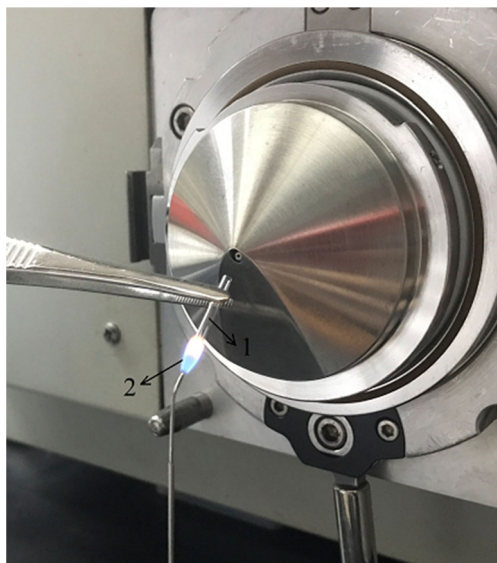


Figure 1. The photograph of fast eruption desorption ionization mass spectrometry (FEDI-MS) apparatus for analysis of the sample. (1) Sample tube. (2) Heating source

analogous to the volcanic eruption. The strong convective and triboelectrification emerged in the eruption process, which gave rise to charge separation and initiated the ionization of analytes. Fig. 2a–b and Figure S4 showed the spectra obtained from the direct analysis of liquid compounds like dibenzosuberone and benzoxazole as well as solid compounds like 3,3',4',5,7-pentahydroxyflavone and phthalide. The intact protonated, sodiated, and potassiated signals were obtained with high-quality FEDI-MS spectra. The formation of Na and K adduction seems not to eliminate sample tube surface as a possible contributor for generating these adduction ions, therefore the frictional electrification [12–14] may be responsible for initiating ionization.

Solvent-free sample preparation of non-assisted eruption mode provides a simple and rapid analytical method. By extensive analysis of various organic compounds, experimental results show that non-assisted eruption mode could analyze stable and volatile compounds but no signal was observed for nonvolatile and fragile compounds, such as organometallic compounds, glycosides, etc. The possible reason is that fragile molecules have been decomposed before desorption and nonvolatile compounds remain no desorption in non-assisted eruption mode.

In order to achieve ionization of nonvolatile compounds, especially organometallic compounds, a substance was attempted to introduce, which not only produced abundant energy to assist the desorption but generated a large number of gases to assist analytes into the mass spectrometer. It was found that the energetic material (EM) [15, 16] was a suitable substance, which simultaneously generates abundant energy and gases by the oxidation reaction and was applied to the next experiment, namely EM-assisted eruption mode. Here, ammonium perchlorate [17, 18], a widely used oxidizer in various propellants and pyrotechnics, was used as an energetic material for EM-assisted eruption experiments. The ammonium perchlorate was first introduced to the sample tube, approximately one fifth of the sample tube, over which solid sample (roughly nanogram scope) was applied. Ammonium perchlorate in excess of the analyte permitted energy to transfer fast from energetic material to the uppermost molecules of analytes. The abundant energy and gases were generated in a small space of sample tube, once exposure of sample tube bottom to the heating source. The high-velocity gases entraining analytes were erupted from the sample tube, which was accompanied by violent collision and friction. The generated energy was high enough to desorb and ionize analytes, especially for nonvolatile compounds. The high-speed gases could assist nonvolatile compounds rapidly into MS for detection. More importantly, there is no signal interference of ammonium perchlorate to the sample because it was eventually decomposed into gases.

Here, several examples of the EM-assisted eruption were presented for direct analysis of the nonvolatile sample (Fig. 2c–d and Figure S5). The intact cation ions were obtained at m/z 772 and m/z 189 for analysis of Piers-Grubbs 2nd and cobaltocene hexafluorophosphate. For analysis of ruthenium

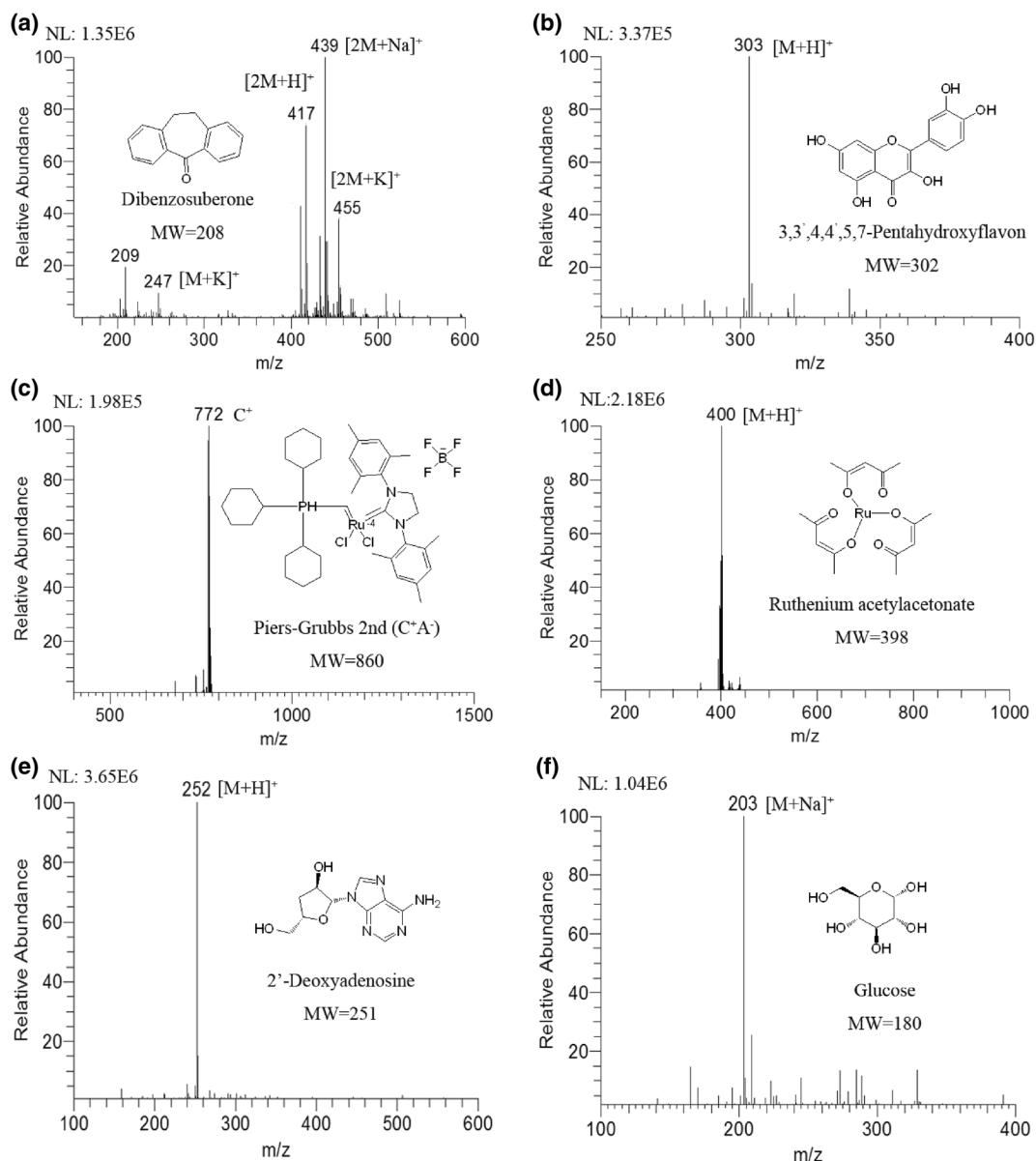


Figure 2. FEDI-MS direct analysis of (a) dibenzosuberone, (b) 3,3',4',5,7-pentahydroxyflavone, (c) Piers-Grubbs 2nd (C⁺A⁻), (d) ruthenium acetylacetonate, (e) 2'-deoxyadenosine, (f) glucose

acetylacetonate and 4-ethoxycarbonylphenyl boronic acid. The intact protonated, sodiated, and potassiated signals were obtained. These results suggest that EM-assisted eruption mode is a beneficial means of direct analysis of nonvolatile compounds, especially for organometallics. However, EM-assisted eruption is still not suitable for analysis of fragile compounds that is liable to fragment in EM-assisted eruption mode.

Consequently, the matrix that could effectively prevent the thermal degradation during the heating process is necessary for analysis of fragile compounds. The solvent was an appropriate matrix for analysis of fragile molecules (Figure S6) since the solvent enables to transfer heating energy from heating source to the analyte, which has the role of mediator. The experiments for direct analysis of various samples in the solvent were performed, which is called solvent-assisted eruption mode. The sample dissolved in the solvent was

introduced into the sample tube. When the heating source touched the bottom of the sample tube, the solvent would rapidly expand thousands of times in a small space and was erupted from the sample tube. In the process of fast eruption, the solvent was ionized firstly and the analytes were ionized by proton transfer reaction, cation transfer reaction, etc. The ionization mechanism is similar to matrix-assisted laser desorption ionization (MALDI) [19], where the solvent was analogous to the matrix in MALDI [20].

The intact ion signals without fragments were presented in Fig. 2e–f and Figure S7 by solvent-assisted eruption for analysis of 2'-Deoxyadenosine, glucose, GLY-LEU, and GLY-LEU. The reason may be that fast eruption renders heated time of sample fairly short and the sample is rapidly desorbed and ionized. Therefore, the evaporation rate of analytes is faster than decomposition rate in the condition of solvent protection.

Moreover, collisional cooling of nascent ions at atmosphere may be conducive to suppress thermal decomposition. These results demonstrate that the solvent-assisted eruption is suited to analyze fragile molecules, which is a softer ionization approach taking into account the solvent protection compared to non-assisted eruption and EM-assisted eruption.

In addition, the limit of detection (LOD) was investigated using solvent-assisted eruption through analysis of 18-crown-6. The LOD was as low as 200 fg (Figure S8), demonstrating the high sensitivity of the FEDI-MS. Therefore the FEDI-MS has the potential to detect trace sample. Then, the real-world samples were analyzed by FEDI without any pretreatment in an open environment. The prewetted tip of sample tube first gently touched the metronidazole tablets or celecoxib capsules, which then was analyzed by using solvent-assisted eruption mode. High-quality spectra were acquired, confirmed by MS/MS mass spectra (Figure S9 and Figure S10). Both above-mentioned experimental results were achieved within several seconds, demonstrating the wonderful applicability of the FEDI for direct analysis of real-world samples. Moreover, the contamination or sample carryover effect was not obvious because the sample was applied in small amounts for FEDI-MS analysis with high sensitivity. In addition, FEDI-MS could also analyze the sample in the negative ion mode (Figure S11). Therefore, the FEDI permits for smooth, fast, and nondisruptive conversion between positive and negative ion modes.

Conclusions

In summary, a simple, rapid, and low-cost ionization technique has been developed. According to compound properties, three analytical modes of the FEDI could be chosen for rapid analysis of various samples without the assistance of the laser and high voltage. Moreover, the FEDI was demonstrated to be applicable to directly analyze complex matrixes without sample pretreatment. All of the above characteristics allow FEDI as an attractive candidate to couple portable mass spectrometers for wide applicability in laboratory and in-field analysis.

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