Improving the Performance of the Mini 2000 Mass Spectrometer with a Triboelectric Nanogenerator Electrospray Ionization Source

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ABSTRACT: Balancing the contradiction between portability and analytical performances of a miniaturized mass spectrometer is vital to extend its on-site applications. In this study, triboelectric nanogenerator (TENG)-driven ion sources were coupled with our home-built Mini 2000 system and applied to the analyses of different samples. Compared with the conventional direct current (DC) nanoelectrospray ionization (nanoESI) source, the ion intensity of the TENG-nanoESI miniature mass spectrometer was improved by ~3 times. Moreover, maybe due to the different pathways of ion formation in comparison with DC electrospray, TENG electrospray is shown to reduce the salt suppression effect during ionization. With these figures of merit, the direct detection of reserpine in saliva was demonstrated using the TENG-Mini 2000 system.

1. INTRODUCTION

Owing to its high sensitivity, molecular specificity, and accurate quantitative analysis, mass spectrometry (MS) has a wide range of applications in biomedicine, food science, forensic field, drug discovery, and other fields.1−5 Commercial in-lab mass spectrometers typically have some disadvantages such as large size, high power consumption, strict working environmental conditions and complex operational procedures,6,7 which limit the use of these MS systems for in-field applications. An ideal instrument for in situ applications should be small and portable. Miniature mass spectrometry broadens its application areas to environmental monitoring, public security, space exploration and personal healthcare.8−12 Besides, a miniature mass spectrometer for in situ detection is also expected to have adequate analytical performances in terms of sensitivity and mass resolution, as well as simplified operational procedures.

Until now, various kinds of miniature mass spectrometers have been developed rapidly, which mainly involve miniaturized mass analyzers,13−16 ion transfer devices,17 and compact electronic and vacuum systems.18−20 A miniaturized ion funnel could increase ion transfer efficiency.17,21 Mass analyzers have also been miniaturized, which could help in terms of reducing the requirements of the electronic system, as well as increasing its tolerance to higher buffer gas pressures.22−25 Ionization is the first step in mass spectrometry; the voltage applied is used to convert neutrals into gas-phase ions for mass analysis.26−28 Conventional direct current (DC) high-voltage power creates ion sources suffering from inherent disadvantages, such as high cost, limited portability and safety concerns.29−31 The recent demonstration that charge pulses can trigger an electrospray ionization (ESI) process provided a new method for developing highly convenient and robust devices to control the ionization process.32−34 Triboelectric nanogenerators (TENGs) are one of the sustainable power sources that can transform mechanical energy into electricity.35−37 Recently, TENG-driven ion sources for mass spectrometric analysis have been reported.38 Small organic molecules and biomolecules were all successfully detected by TENG-ESI MS. TENG ion sources not only improve the sensitivity of analysis but also avoid the destructive corona discharge phenomenon while electrospraying solutions with high surface tension under high voltages.39

In this work, we report a TENG-driven ion source integrated with our home-built Mini 2000 system12,17,40 for the analysis of a wide range of chemical compounds, ranging from small organic molecules to large biomolecules. TENG-ESI showed enhanced sensitivity and high salt tolerance. Reserpine in saliva or human serum without pretreatment was successfully detected by TENG-Mini 2000, which is an improvement for
2. EXPERIMENTAL SECTION

2.1. Chemical Samples. Peptide Met–Arg–Phe–Ala (MRFA) (MW 524) and protein cytochrome c were purchased from Sigma-Aldrich (St. Louis, MO). Reserpine (MW 609) was purchased from Acros Organics (NJ). High-performance liquid chromatography-grade methanol was purchased from Fisher Scientific (Fairlawn, NJ). Purified water was obtained from Wahaha (Hangzhou, China). Saliva and serum samples were collected from normal volunteers. The MRFA solution used in experiments were all dissolved in methanol/H2O (1:1, v/v), and the protein sample was prepared in 1:1 (v/v) methanol and deionized water with addition of 1:1000 formic acid.

2.2. Fabrication and Operation of TENGs. The TENG was prepared by physical vapor deposition of 1 μm aluminum on a 50 μm-thick poly(vinyl chloride) (PVC) film, forming two 75 × 60 mm² rectangular areas separated by a 75 × 1 mm² uncoated rectangular region (as shown in Figure 2a). And then the PVC was mounted on the acrylic. The movable TENG part consists of an Al foil (55 × 65 mm²), a piece of sponge, and an acrylic board. In the process of operating the TENG, the movable parts were mounted on a linear motor, and the static part was fixed onto a stage. These two parts are mounted face to face to ensure an optimal contact between the PVC surface and the Al foil. High-frequency pulses were generated by rapidly switching the sliding direction at a defined sliding speed. The output voltage of the device was very stable throughout the experiments.

2.3. Mini Mass Spectrometric Analysis. As shown in Figure 1a, the home-built mini-MS was constructed with a two-stage vacuum chamber maintained by a differential pump system. The first vacuum is realized by a diaphragm pump (50 L/min, SVF-E0-50, Scroll Tech Inc., China), and a turbo pump (80 L/s, Hipace80, Pfeiffer Inc., Germany) is installed on the second chamber to further improve the degree of vacuum. A linear ion trap with hyperbolic electrodes (x₀ = y₀ = 4 mm, z₀ = 40 mm) was placed in the second vacuum stage. The ion detector consists of a home-built dynode used to generate secondary electrons and an electron multiplier (model 2500, Detech Inc.) to amplify the signal. The first vacuum chamber is connected to atmosphere by a stainless-steel capillary (length of 10 cm and inner diameter of 0.25 mm), and a pinhole (length of 1 mm and inner diameter of 0.4 mm) was placed
between these two vacuum chambers. An external high-voltage interface can provide DC voltage (0 to ±5000 V), which was used for the ionization source. A platinum electrode is inserted inside the tips of the capillaries used as nanoelectrospray ionization (nanoESI) sources. The photo of this mini-MS (Mini 2000) is shown in Figure 1b, which has dimensions of 38 × 23 × 24 cm³ (length × width × height). DC-nanoESI/TENG-nanoESI measurements were also conducted by Mini 2000 using the same electrospray emitter tip.

3. RESULTS AND DISCUSSION

3.1. Working Mechanism and Performance of TENG. Figure 2b shows the working mechanism of the freestanding-mode TENG; the alternating flow of electrons is generated between the triboelectrification and electrostatic induction electrodes. When Al contacts PVC, electrons will be injected from the Al surface to the PVC film, due to the differences in the ability to attract electrons. As the movable part slides forward (from state i to state ii), the tribo-charges in the interface regions are separated, resulting in a higher potential in the right electrode than that in the left one; thus the

Figure 3. Linear quantitation curves for MRFA with a LOD of 50 ppb for DC-nanoESI and 10 ppb for TENG-nanoESI are shown in (a). TENG-nanoESI (b, d) are compared to conventional nanoESI spectra (c, e) obtained with 500 ppb MRFA and 10 ppb MRFA, respectively.

Figure 4. (a) Different electrospray ionization mass spectra of MRFA in methanol/H₂O (1:1) obtained from 0, 1, 10, and 25 mM NaCl solution. TENG-nanoESI spectra (b, d) are compared with conventional nanoESI spectra (c, e) obtained in MRFA without Na⁺ and 25 mM Na⁺ solution, respectively.
electrons will be driven, flowing from the left electrode to the right one through the outer circuit (meaning a current flow in the reverse direction, as shown in Figure 2b-ii). In this process, electrons keep moving until the movable part reaches the right edge of the static plate, which is demonstrated in Figure 2b-iii. At that instant, the amount of transferred charges between the two electrodes reaches the maximum value. As the movable part moves back, the electrons will flow back from the right electrode to the left one (Figure 2b-iv). Therefore, the entire process results in an alternating-current pulse output. The output performance is plotted in Figure 2c,d. It is found that the device outputs a voltage of around 1400 V, and the amount of transferred charges was about 272 nC.

3.2. Analyses of MRFA. Operated in a pulsed fashion, higher ionization efficiency was achieved using the TENG-driven nanoESI. When integrated with our home-built miniature mass spectrometer (Figure 2b), the analytical performance of the mini-MS was expected to be improved. First, a 500 ppb MRFA sample was tested using the standard DC (1 kV) nanoESI method. In comparison, the TENG (~1.4 kV) nanoESI using the same nanoESI emitter could enhance the ion intensity by 3−4-fold at the same concentration level (Figure 3b,c).

To evaluate the sensitivity of the system, we chose the commonly used peptide, MRFA. In the experiments, different concentrations of MRFA were detected in both standard DC-nanoESI and TENG-nanoESI modes with the same nanoESI emitter. Unless otherwise specified, the parameters of the instrument remain unchanged. The quantitative curves of MRFA are shown in Figure 3a. Limit of detection (LOD) values of 10 and 50 ppb MRFA were obtained with TENG-nanoESI and DC-nanoESI, respectively. Figure 3d,e plot the corresponding mass spectra at 10 ppb using TENG-nanoESI and DC-nanoESI, respectively. To ensure the reliability, at least three repeated tests with different spray tips were carried out under each condition and a S/N ratio of 5 was maintained in each test.

To fully demonstrate the feasibility of TENG-nanoESI under salt buffer applications, MRFA in methanol/H2O (1:1) with different concentrations of NaCl solution (1, 10, and 25 mM) was further analyzed. In this case, the observed peaks were predominantly [M]+ (m/z 524) and [M + Na]+ (m/z 547). As indicated in Figure 4d,e, compared with DC-nanoESI, a better signal intensity with a 2-fold sensitivity improvement of MRFA could be achieved by TENG-nanoESI, whereas there is no enhancement of the [M + Na]+ signal intensity in the high sodium salt solution (25 mM Na+).

3.3. Analyses of Protein. Due to the miniature electronic systems, the mass range of the Mini mass spectrometer is lower than the commercial MS instruments in labs. Therefore, it could be detected by increasing the charges of large biomolecules. However, the mass spectra are still not satisfactory within the mass range of Mini 2000. In this experiment, cytochrome c was selected to verify the performance of the instrument. Upon using the TENG-driven nanoESI source, well-resolved charge state distributions of cytochrome c primarily produced from the 11+ to 16+ charge states were observed in Figure 5a. In comparison, for the same sample using the traditional DC-nanoESI source, charge state distributions from 12+ and 15+ were detected with lower intensity (Figure 5b). Results indicated that the TENG-nanoESI source could improve the performance of the Mini 2000 instrument in terms of detecting proteins.

3.4. Direct Analyses of Drug in Saliva and Human Serum. Practical samples, such as saliva and human serum, have very complex matrices. Surface-assisted laser desorption ionization-mass spectrometry was developed for testing of illicit drugs in saliva, urine, and blood. However, direct analysis of drug in saliva or serum by ESI-MS remains a great challenge. Conventionally, complicated sample pretreatment procedures, including chromatography and some microextraction techniques, are performed before MS analysis. However, in practical detection using a miniature mass spectrometer, the sample pretreatment equipment is very restricted. Therefore, it is very ideal to handle these complex samples directly with minimum sample pretreatments.
The TENG-nanoESI-coupled Mini 2000 has shown enhanced ion intensity and low sodium suppression effect. Therefore, the TENG-nanoESI-integrated Mini-MS was further tested to analyze real samples without any sample pretreatment. As a demonstration, reserpine was spiked into saliva and normal human serum. Prior to analysis, the saliva stock solution was mixed with the same volume of methanol/H₂O (1:1 v/v), whereas human serum was not diluted. Then the untreated saliva and serum were directly tested by Mini 2000, as shown in Figure 6. Reserpine in saliva (Figure 6a,b) and normal human serum (Figure 6c,d) was detected by DC- and TENG-driven nanoESI sources, respectively. Upon using the DC-driven mode, no reserpine signal was obtained. However, a satisfactory signal can be observed for reserpine (m/z 609) in saliva and serum at a final concentration of 5 ppm upon using the TENG-driven mode. Results suggest that the TENG-nanoESI source coupled with the Mini 2000 could be applied in applications of complex sample analysis with minimum sample pretreatment. The underlying mechanism of TENG-nanoESI is similar to that of alternating current or pulsed voltage-triggered ESI. The alternatingly induced voltage generates quasi-simultaneous production of both positive and negative ions. The electric field generated within the liquid flow would drive ions flowing toward or away from the ESI tip, which depends on the charge polarity and electric field direction. This electric field would have stronger effects on smaller ions, such as salt ions, since they would travel longer distances, and therefore, setting up a separation and cleaning effect.

4. CONCLUSIONS

In summary, TENG-nanoESI has high salt tolerance, good reproducibility, and could improve the sensitivity of Mini 2000. As a demonstration, reserpine in saliva and serum was directly detected using the TENG-nanoESI and Mini 2000. TENG is a suitable ion source for portable mass spectrometers, which opens the door for further applications of direct complex sample analysis.

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Notes
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