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Short communication

A novel strategy based on the dielectric barrier discharge plasma for rapid elimination of the carryover associated with μPESI-MS/MS system

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In mass spectrometry (MS) analysis, carryover is a common and unavoidable problem. It causes over-estimation of analyte levels, which significantly influences accuracy and precision. Therefore, there are strict limits on carryover in MS-based assays. The conventional capillary-based electrospray ionization (ESI) restricts the use of MS for real-time monitoring, where a prompt response is crucial. Recently, we have developed a micro probe electrospray ionization (μPESI) coupled with MS (μPESI-MS) technology, enabling MS analysis within 40 s without a chromatographic column [1]. However, the challenge of carryover arises when trying to make the micro probe reusable for resource-saving purposes. Considering that dielectric barrier discharge (DBD) plasma is effective in degrading contaminants in water and gas [2], we hypothesized the eventual use of the DBD plasma to "wash" the micro probe. Then, a DBD plasma wash tube (DBD-WT) was introduced for rapid carryover elimination in μPESI-MS analysis.

The main experimental apparatus consists of a high-voltage power supply and a plasma reactor. The plasma reactor contains a ceramic tube, a T connector, a union, and nuts. The ceramic tube served as the dielectric layers, while a metallic nut and the aluminum film pasted on the ceramic tube served as electrodes. The power supply provided an adjustable frequency from 15 to 45 kHz and a voltage from 1 to 10 kV. The schematic diagrams of the DBD-WT washing device and the experiment platform are shown in Fig. 1A. Micro probe washing experiments were carried out in parallel with both DBD-WT plasma washing and MeOH washing. The washing procedure is detailed in the Supplementary data.

The crucial factors affecting DBD-WT performance included washing cycles, gas flow rate, and media gas [3]. We examined the impact of these factors on reserpine (RSP) at 1000.0 ng/mL, varying one factor at a time while keeping the others fixed at their optimal values.

The results (Table S1) demonstrated that for washing cycles, twice of DBD-WT washing could reduce the carryover to meet the industrial criterion (<0.05%) [4]. However, the MeOH washing method showed much poorer performance. For the flow rate, it appeared to have minimal effect on the carryover of the micro probe. On the other hand, the type of media gas significantly affected the elimination efficiency. Effective washing was only achieved by DBD-WT with oxygen-rich media gases. Pure nitrogen, argon, and helium were all not suitable for DBD-WT for carryover elimination.

Two types of RSP standard solution (500.0 ng/mL) were prepared, spiked with or without 1.0 mg/mL 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) (as the free radicals capturer [5]), each in triplicate. Using compressed air as the media gas, the plasma was transported from the adjusted setup of DBD-WT (Fig. S1) into each

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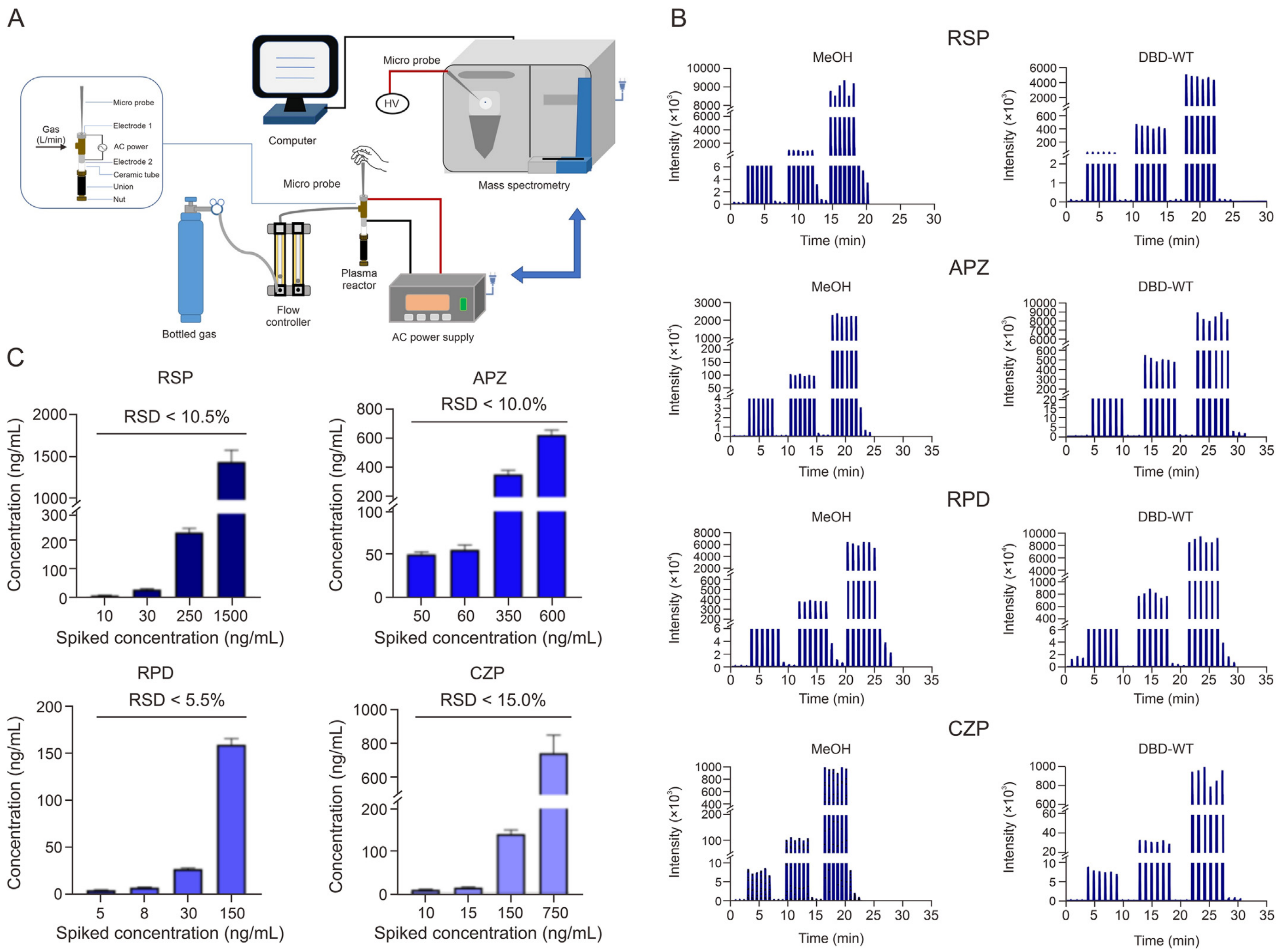

Fig. 1. The apparatus installation and analysis performance of dielectric barrier discharge (DBD) plasma wash tube (DBD-WT). (A) Schematic diagram of the experiment platform. (B) The carryover elimination efficiency of MeOH method and DBD-WT method on reserpine (RSP), aripiprazole (APZ), risperidone (RPD), and clozapine (CZP) by micro probe electrospray ionization (μPESI) tandem mass spectrometry (μPESI-MS/MS). (C) The accuracy of four analytes determined by the μPESI-MS/MS using the DBD-WT washing method (n = 6). AC: alternating curren; HV: high voltage; RSD: relative standard deviation.

RSP solution for 5 s. The RSP intensity was measured by the μPESI-MS system before and after DBD-WT plasma treatment.

The elimination efficiency of the RSP solution was notably higher in the absence of TEMPO (shown in Table S2), indicating that free radicals were necessary for the DBD-WT washing performance.

Two fluorescent probes, BBoxiProbe O11 and BBoxiProbe O52, were adapted to detect the production of the reactive oxygen species (ROS) and reactive nitrogen species (RNS) in the plasma under different media gas atmospheres. The plasma was introduced into the fluorescent probe solutions, and the fluorescence intensity was measured at its characteristic wavelength. Compressed air and oxygen generated significantly higher levels of ROS and RNS compared to other gases (Fig. S2).

These results demonstrated the correlation between the carryover elimination efficiency and the production of reactive species in the DBD-WT plasma.

Apart from RSP, aripiprazole (APZ), risperidone (RPD), and clozapine (CZP), which have different physical and chemical properties, were selected for the DBD-WT carryover elimination performance assay. Furthermore, the quantification of RSP, APZ, RPD, and CZP in rat plasma was carried out to validate the carryover elimination performance of DBD-WT in μPESI-MS analysis. Six to seven sets of QC samples were randomly interspersed among the calibration curve samples, to mimic unknown samples (Fig. S3).

Compared to the MeOH method, the DBD-WT method exhibited much lower carryover for these four representative analytes (chromogram in Fig. 1B and data in Table S3). The accuracy of these four analytes determined by the μPESI-MS using the DBD-WT washing method were all acceptable, as shown in Fig. 1C, the concentration levels of calibrators and QC samples were shown in Table S4, and the MS parameters for the four representative analytes were shown in Table S5.

In summary, this study demonstrated that DBD-WT is highly compatible with the μPESI-MS system, providing a rapid micro probe washing strategy to make the micro probe reusable, speed up the analysis efficiency, and enable real-time analysis.

CRediT authorship contribution statement

Qian Liu: Writing – original draft, Methodology, Investigation, Funding acquisition. **Simin Zhang:** Writing – original draft, Validation, Investigation. **Xiangyang Qu:** Validation, Methodology. **Yunhui Xing:** Validation, Methodology. **Zhenwei Xiao:** Methodology, Investigation. **Shicheng Fan:** Validation, Methodology.

Janshon Zhu: Resources, Project administration. **Min Huang:** Resources, Project administration. **Huichang Bi:** Writing – review & editing, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that there are no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpha.2024.101017.

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