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Electro-Filtering Paper Spray Ionization Method

Fangling Wu[1,2], Chuan-Fan Ding[1,2]*

[1]Institute of Mass Spectrometry, School of Materials Science & Chemical Engineering, Ningbo University, Ningbo, Zhejiang, China
[2]Department of Chemistry, Fudan University, Shanghai, China

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***Correspondence:**
Prof. Chuan-Fan Ding, Institute of Mass Spectrometry, School of Materials of Science & Chemical Engineering, Ningbo University, Ningbo, Zhejiang, China; Telephone No: +86-0574-87605710; Email: dingchuanfan@nbu.edu.cn.

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Abstract

A relatively rigid and good electrical conductive copper filter severed as a substrate for the paper spray named Electro-Filtering Paper Spray Ionization (EFSI) is mini reviewed. The copper filter is used to increase the conductivity and pressure tolerance for the paper substrate, which can insure sufficient, efficient and direct sample-solvent extraction for different types of solid samples, and also a low voltage is required for paper spray. The capability and reliability of EFSI-MS were demonstrated experimentally for indirect high-throughput component analysis or the desired ion signals for a wide range of solid samples by selecting and optimizing different extraction solvents, which is not feasible with conventional ESI or direct paper spray methods. Simultaneously, trace targeted substance for the large-volume sample can be effective extracted and pre-concentration by the optimized solvent for direct mass spectrometry analysis with no or extremely minimal sample preparation effort for the EFSI method. Besides, with the attractive features of cost-effectiveness, rapid, process simplicity and high-throughput, the potential and novel applications of the EFSI-MS or EFSI-MS-MS can focused in the fields of environment, bio-science, food safety, and in-vitro diagnostics in clinical routine analysis are expected in the future work, where substantial time and labor could be saved when investigating the potential causes of disease.

Introduction

Mass spectrometry (MS) is a powerful analysis technology, providing information on molecular weight and chemical structures of the analytes in different field[1-3]. Ion source is a critical part of the MS, and for the primal and widely used ion source such as electrospray ionization (ESI)[4, 5], complex sample preparation or routinely chromatography separation is required for the complex practical samples before the MS measurement. However, the development of desorption electrospray ionization (DESI) by Cooks et al. in 2004[6], and then the introduction of direct analysis to real time (DART) by Cody and co-workers in 2005[7], which were the pivotal milestones in the development of a subfield of MS analytical known as ambient ionization MS (AI-MS)[8, 9]. This new ionization method of AI-MS has greatly altered the traditional analysis that allowing sample analysis requiring no or minimal sample preparation, and it takes place in the atmospheric pressure in a quick, simple, and effective manner. Then, many other sub-group of AI methods were developed to address the need for rapid and direct analysis of practical samples subsequently, such as desorption atmospheric pressure chemical ionization (DAPCI)[10], plasma-assisted desorption/ionization (PADI)[11], dielectric barrier discharge ionization (DBDI)[12], atmospheric pressure solids analysis probe (ASAP)[13], electrospray-assisted laser desorption ionization (ELDI)[14], matrix-assisted laser desorption electrospray ionization (MALDESI)[15], laser ablation-electrospray ionization (LAESI)[16], and infrared laser-assisted desorption electrospray ionization (IR-LADESI)[17]. In addition, many other new AI methods characterized by the generation of an electrospray directly from the sample were investigated, such as paper spray electrospray ionization (PS)[18-21], extractive electrospray ionization (EESI)[22], wooden-tip electrospray ionization[23], and ultrasonic surgical aspiration and sonic spray[24].

The aforementioned AI methods, PS is interesting described as a direct ionization method employing cellulose based materials of paper, first developed by Cooks and Ouyang groups in 2010[19]. PS is built on a piece of triangular paper, held by a metal clip and positioned in front of the MS orifice. Analytical sample is placed on the middle of the paper triangle, and the electrospray ionization generated by wetting the paper substrate with solvent. Overall, the PS-MS method shows great promises for quantitative analyses for a number of applications, due to the high matrix tolerance and simple operation, especially for the illicit drugs in blood sample [20]. However, some weaknesses have existed on the method of PS, such as it was easily deformed when subjected to high pressure that it cannot bear a large volume sample. Paper electrospray is the ionization of the analytes by conduction through a solvent on the paper substance, which the paper should be wetted during the analysis process. In this way, some other AI methods were developed based on PS method, such as aluminum foil electrospray ionization[25], leaf spray[26], and paper cone spray ionization[27].

Electro-Filtering Paper Spray Ionization

Electro-Filtering Paper Spray Ionization (EFSI) method was also developed on based of PS and validated by our group[28, 29], which a metal filter is served as substrate for the paper spray. The scheme of the EFSI described in Figure 1c[29]. A trungkoni-like filter shape was papered by copper sheet, with 12 mm for height, 10 mm for top radius and 5 mm for radius at the base. A piece of chromatography paper cut into a triangular shape with 30° angles was held by the copper filter, and the length of the paper to the copper top filter was 5 mm. The tip of the paper was directly facing the inlet of the mass spectrometer, the EFSI device was oriented approximately 30° to the horizon, and the distance between the filter-paper tip and the MS inlet was 3-5 mm. Sheath gas (nitrogen, 99.999%) at a flow rate of 0.2–0.5 L min^{-1} was used to facilitate the solid-liquid extraction process and allow rapid infiltration of the analytes into the chromatography paper for separation and spray analysis.

Some distinct advantages can be described for the method of EFSI, such as economic, quick, and high-throughput analysis for large-volume unprocessed practical mixtures. Meanwhile, good electrical conductivity of the electro-filtering made by metal sheet severs as substrate for the paper, resulting in a low voltage was required for paper spray and no solvent was required to wet the paper substance compared to separated paper spray method (Figure 1a)[21] and paper cone spray ionization (Figure 1b)[27]. Analytical sample was incubated in the electro-filter, where a big conductive area for the analysis sample, and the paper spray can be strengthened. Besides, enough interspace for sample incubation can avoid the clogging problems for the EFSI method, which was often encountered in capillary based ESI. As it well known that, trace substance analysis often needs high sensitivity instrument or the complex sample pre-concentration process before detection[30]. Additionally, relatively rigid copper filter can sustain large size practical sample for direct sample-solvent extraction, the trace substance can be released and pre-concentration from the sample for MS analyzed directly.

Influencing factors on the performance of the Electro-Filtering Paper Spray Ionization method

For EFSI, a sheet metal was prepared as an Electro-Filtering and served as substrate for paper spray to bear more pressure for analytical sample, as well as strengthen the conductivity of the paper spraying. Moreover, sample-solution extraction processing can be realized for loading samples of the EFSI owing to the metal electro-filter. Variation in absolute signals complied with using different types of iron sheet, aluminum sheet, and copper sheet, in which EFSI prepared by copper sheet yielded the best MS signal intensity. This is mainly because copper sheet possesses the highest electrical conductivity and it was hard to be oxidized compared to iron sheet and aluminum sheet[31], resulting from the EFSI prepared by copper sheet

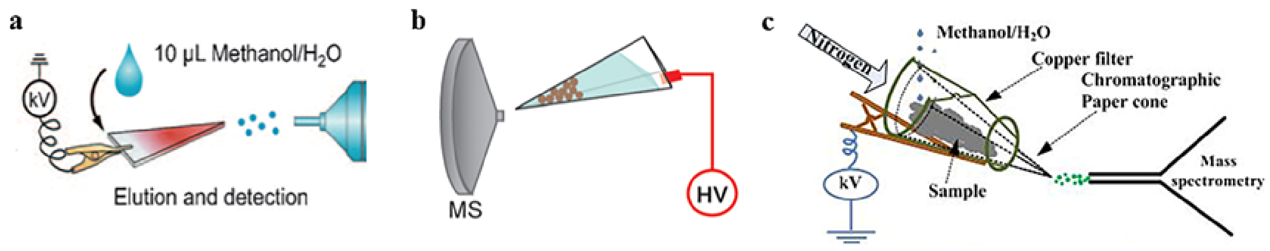

Figure 1: Structural of the (a) paper spray[21]; [b] paper cone spray ionization[27]; [c] Copper Electro-filtering spray ionization source[29]

corresponds to higher ionization efficiency. Analogous to the PS method[32], it was demonstrated that the paper types also influenced to the spray or detection signal of the analytes by the EFSI method. Various paper substances of filter paper with different pore sizes, weight paper and chromatography paper, in which chromatography paper was regarding the optimum choice for the most favorable physical and chemical properties for obtaining the lowest chemical noise and best MS spectra. Besides, types of extraction solvent, solvent volume and extraction frequency are also impacting the detection results. Extraction solvent is not only effect on the release of analytes from complex sample matrices, but also important to spray efficiency for the analytes. In general, organic solvent mixed with water is commended to be used as an extraction solvent[33], in which the commonly used organic solvents are methanol, acetonitrile, acetone, dichloromethane etc.[34,35]. According to the theory, the extraction solvent should be as small as possible to eliminate reductions in analyte distribution constants, and the organic solvent content should above or equal to 50 vol%, which is beneficial for the sample spray and to ensure the high detection sensitivity. Extraction frequency is one of the most crucial steps related to extraction time, and extraction frequency is always a compromise between the solvent volume, sensitivity and reproducibility of the analytical method. Some other parameters, such as sheath gas (N_2) flow rate and the electro-filtering temperature can also affect the extraction efficiency. Typically, it is necessary to optimize the favorable extraction condition by experiment properly according to the diverse analytical sample.

Applications of the Electro-Filtering Paper Spray Ionization-MS

EFSI-MS shows great promise for quantitative and qualitative analyses for different practical samples, including target and non-target compounds of small biomolecules, protein or polypeptide molecules in solid, liquid, and powder samples. At present, EFSI-MS was success to analyze target analytes, such as antibiotic in complex animal products, reserpine and Cytochrome C in soil sample[28,29]. Evaluating the results from the EFSI-MS method were better consistency with the ESI result, and the precision obtained for reproducibility was 81.6%–96.3%, and recoveries were 75.0%–94.6%. Simultaneously, EFSI-MS was also applied to the non-target analysis in practical samples of apple, pork, coffee, and green tea (dried), in which good MS spectra of vitamins, tannins, mineral salts, organic acids, and carbohydrates (molecular weight within 400) were detected for apple; some multivalent compounds of polypeptide or protein in the pork was detected in pork; the main adduct ions of coffee ingredients such as caffeine and dipotassium phosphate or arginine were detected in coffee sample; by changing the extraction solvent, different MS spectra were appeared for the green tea (dried) of method/water and acetone/water. The result reveals that the mass of the target compounds in practical samples can be obtained by optimizing the extraction solvent. In addition, the method of EFSI-MS can avoid the possibility of loss or contamination of analytes during sample pre-treatment, and the method also displays accept accuracy and stability. Because EFSI can withstand large volume samples, that it can be applied to trace substance analysis by adding the analytical sample volume. Besides, low ionization voltage and simple device are required for the EFSI method, that it can be applied to vivo analysis by combined with mini mass spectrometer[36]. Otherwise, the potential and novel applications of the EFSI-MS or EFSI-MS-MS can focus in the fields of proteomics, metabolomics, biomarker discovery, and in-vitro diagnostics in clinical routine analysis are expected in the future work, where substantial time and labor could be saved when investigating the potential causes of disease.

Conclusion

In this mini review, the incorporate of a relatively rigid and good electrical conductivity copper filter for loading different types of analytical samples for effective sample-solvent extraction processing, as well as to strengthen the conductivity of the paper spraying. The method is applicable for indirect analysis of large-volume unprocessed samples, which cannot be achieved through conventional ESI or direct paper spray methods. Besides, EFSI-MS can generate the desired ion signals for a wide range of compounds by selecting and optimizing an appropriate extraction solvent. And the trace substance direct analysis for large volume sample can be realized by efficient and alternative sample-liquid extraction process. Additionally, with the attractive features of rapid analysis, high-throughput, cost-effectiveness, and process simplicity, that the method of EFSI-MS can be a potential alternative for effective targeted or component trace analysis of unprocessed practical samples by adding the sample volume, or even the biological tissue samples in clinical routine analysis.

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