A 3D-PRINTED MINIATURIZED ION SOURCE FOR MASS SPECTROMETRY BASED ON PAPER SPRAY IONIZATION WITH INTEGRATED, PASSIVE FLUID CONTROL

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ABSTRACT

3D-printed cartridges were designed and fabricated to improve the paper spray ionization method for mass spectrometry (MS). The cartridges protect the fragile paper material, stabilize the tip to prevent warping and misalignment and facilitate interfacing with mass spectrometry. Most importantly, the cartridge enables sophisticated control over solvent flows. Integrated wetting features enable fast initial wetting (in approximately one minute) and subsequent controlled and continuous solvent supply (for almost an hour). Analysis of a small molecule (lidocaine) has been demonstrated. This work creates possibilities for the analysis of slowly eluting compounds, online paper chromatography-MS and easy on-site sampling.

KEYWORDS: paper spray ionization, capillary action, 3D-Printing, spray time

INTRODUCTION

The fabrication and characterization of a 3D-printed miniaturized ion source for mass spectrometry (MS) are presented in this work. Sophisticated, passive solvent control was designed into the cartridge and tested for user-friendly sample analysis with MS outside the usual clinical environment.

The source is based on the ambient ionization technique paper spray ionization (PSI) [1], in which sample is applied to a piece of paper cut into a sharp tip. Subsequent application of solvent and a high potential results in the generation of ion spray. Major advantages of PSI are low cost, applicability in ambient environment and easy sample analysis.

The authors of the original PSI method report that spray could be generated for roughly one minute only [1]. Previously suggested solutions to this problem are the use of a pump for continuous solvent application [2], or passive solvent supply via a hydrophilic wick suspended in a beaker with solvent [3]. However, these approaches increase bulkiness of the setup, and decrease user-friendliness and reproducibility. The cartridge reported in this work can provide immediate and extended spray, yet is no larger than a thumb and easy to use. A cartridge for PSI has been reported previously [4]; however, its sole purpose was to provide physical stability and protection to the paper tip.

EXPERIMENTAL

Designs for the cartridge were made with SolidWorks and fabricated in polylactic acid (PLA) using a hot extrusion-based 3D-Printer. The iterative design-fabricate-test-evaluate process was focused on producing a cartridge which would: (1) protect the paper tip from damage and deformation; (2) facilitate positioning in front of MS equipment; (3) provide good control over solvent distribution to the paper tip. This meant that the initial wetting should occur rapidly, yet that there should be a continuous and controlled supply of solvent afterwards.

Wetting characterization of the cartridge was performed by measuring wetting times (i.e. the time required to fully wet the paper tip) and wetting volume (i.e. the amount of solvent that was guided to the tip in the initial wetting phase) for a number of aqueous solvent mixtures with either methanol (MeOH) or acetonitrile (ACN).

Next, the PSI cartridge was used first to generate prolonged spray with a water/acetonitrile/formic acid (50/50/1) mixture and then for the MS (quadrupole) analysis of lidocaine (1 µL of 1 mM solution in water applied on the front of the tip) with methanol/water/formic acid (90/10/1) as solvent.

RESULTS AND DISCUSSION

The ion source reported in this paper (Figure 1) was designed to enable fast initial wetting and passive, continuous solvent supply to the paper tip. As a result, the cartridge can be used almost immediately for analysis after filling a dedicated reservoir with solvent, as well as spray for tens of minutes without using pumps.

![Cartridge schematic](image)

Figure 1. (A-B) Photographs of the bottom (with paper tip; iii) and top parts of the cartridge, respectively. (C) Schematic representation of the bottom part. (D) schematic representation of an entire cartridge. The central hydrophilic wick (i), connected to the paper tip, is suspended over a beam (3) in the reservoir (1) and is in constant contact with a solvent guide structure (5) on the cartridge top. (E) When the level of solvent is initially high, this paper-PLA combination is in contact with the solvent and fast fluid movement between them is possible. (F) After a fixed amount of solvent has traveled to the paper tip, the connection is broken and the fast supply ceases. A second hydrophilic wick (ii), which is suspended over a cavity (6) and onto the bottom of the reservoir, ensures continuous solvent supply (wick (ii) not visible in C-F).

The mechanism for fast wetting, based on capillary action of solvents through the paper, as well as the much faster movement of solvent between the wetted paper and the PLA, is explained in Figure 1. The latter mechanism initially enables fast transport of fluids, and stops when the solvent level in the reservoir drops below a certain height. A second hydrophilic wick, suspended over a cavity (i.e. free of contact with PLA) and subsequently to the bottom of the reservoir, ensures continuous solvent supply to the paper by capillary action to maintain ion spray.

Figure 2 shows the wetting times for methanol or acetonitrile mixtures with water, as well as the amount of solvent drawn to the paper tip upon initial wetting. It demonstrates that wetting times decrease as the organic solvent content increases, which can be explained by the improved wettability of PLA. It also proves that the amount of solvent drawn to the paper tip can be controlled.

Next, the cartridge was used for MS experiments. Figure 3A shows the extracted ion chromatogram for an acetonitrile peak, which proves spray could be generated for over 50 minutes. Figure 3B shows a mass spectrum obtained in the analysis of lidocaine, demonstrating that a therapeutic agent spotted onto the paper could be eluted and detected.
Figure 2: Graphs showing the time it takes to fully wet the paper tip (left y-axis) and the amount of solvent drawn to the paper tip upon initial wetting (right y-axis) as functions of the organic solvent content in a solvent mixture with water for methanol (MeOH) and acetonitrile (ACN). 480 µL of solvent was used per experiment. Error bars show standard deviations (n=3 per data point).

Figure 3: (A) Extracted ion chromatogram for an acetonitrile peak (m/z 105; 2M + Na\(^+\)) in a spray experiment with water/acetonitrile/formic acid (50/50/1) and (B) a mass spectrum in the analysis of lidocaine (m/z 235; M + H\(^+\)) from a PSI cartridge with water/methanol/formic acid (10/90/1).

CONCLUSION

A cartridge for PSI was designed and produced. It can provide spray shortly after solvent application and continuously thereafter for over at least fifty minutes. The cartridge has successfully been applied to the analysis of a small pharmaceutical agent. Future work will focus on increasing spray stability for better reproducibility.

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REFERENCES


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