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Direct ion generation from swabs☆

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ABSTRACT

Medical swabs are used for biofluid and tissue sampling in clinical applications. The use of medical swabs as electrospray ionization probes for direct mass spectrometric analysis is a novel and potentially widely applicable development. Here we discuss ion generation, characterize ionization behavior via microscopic videography and describe some illustrative examples of applications.

1. Introduction

New methods of ion generation which simplify analysis and reduce cost are needed for the next generation of mass spectrometry applications, e.g. point of care medicine and in situ drug testing. During the fifteen-year development of ambient ionization methods, over 80 techniques have been reported [1], and these address the need for ion generation under native atmospheric conditions (temperature, humidity, pressure) and with minimal to no sample preparation. A continuing trend, first seen in desorption electrospray ionization (DESI), is the integration of sampling and ionization into a single device. This has resulted in such new methods as rapid evaporative ionization [2], the masSpec Pen [3], liquid microjunction surface sampling probe [4,5], probe electrospray ionization (PESI) [6–8], touch spray (TS) [9,10], paper spray (PS) [11–13], and coated blade spray (CBS) [14–17]. Techniques like PS and CBS are examples of substrate-spray technologies [17]. As recently stated by Gómez-Ríos et al., the operational principle consists of supplying liquid to wicking materials, such as paper strips, and then applying a high electrical field to generate gaseous ions from sharp features of the material via electrospray ionization (ESI) or ESI-like mechanisms [17]. The conditions under which ESI occurs have been well characterized [18–20], even though a universal mechanism of ionization remains to be detailed. The basic criterion is the establishment of a strong electric field that overcomes the surface tension of the analyte-containing solution. A number of parameters influence this criterion including solvent surface tension, solvent conductivity, solvent flow rate, voltage applied to the electrospray emitter, radius of electrospray emitter, distance from the electrospray emitter to ground. The desired result of parameter selection is the generation of a Taylor cone and a stable cone-jet mode electrospray plume. The electrospray plume expels analyte-containing charged primary solvent droplets that undergo evaporation and Coulombic fission beyond the Rayleigh limit and yield gas-phase analyte ions [18–20].

In 2014, we developed swab touch spray (STS) as another example of substrate-spray ambient ionization. In this method, a sample, either solid or liquid, is transferred to a swab tip by gentle touch; ions are subsequently generated upon application of solvent to the swab tip and of a high voltage directly to the swab handle [21–26]. Swabs are ubiquitous, easy-to-use, and inexpensive sampling devices which are used widely in clinical microbiology, cytology, DNA testing, and forensics. Applications that are best tailored for STS are those relying on in vivo, rapid, minimally invasive sampling of minute amounts of sample (e.g. biofluid and tissue), and for which swabs are already the preferred means of sampling. Swab tips are usually made of cotton, rayon, polyester or foam in fused shapes of different dimensions. Medical swabs are designed to reduce bleeding at touch and invasiveness of sampling, to reach superficial wounds or deep body orifices, to achieve high absorption capacity, and to transfer quantitative volumes of fluids. Hence, the potential utility of generating ions directly from medical swabs for rapid and direct MS analysis is substantial and can be done without altering the swab design (i.e. shape, dimension, material) that is already fit for purpose. This makes swabs unconventional ESI emitters with irregular geometries and uncommon dimensions (i.e. overall swab radii are on the order of mm – typical ESI emitters radii are µm).

A number of STS applications have been reported already in the literature including the detection of microbial lipids from cultures [21],

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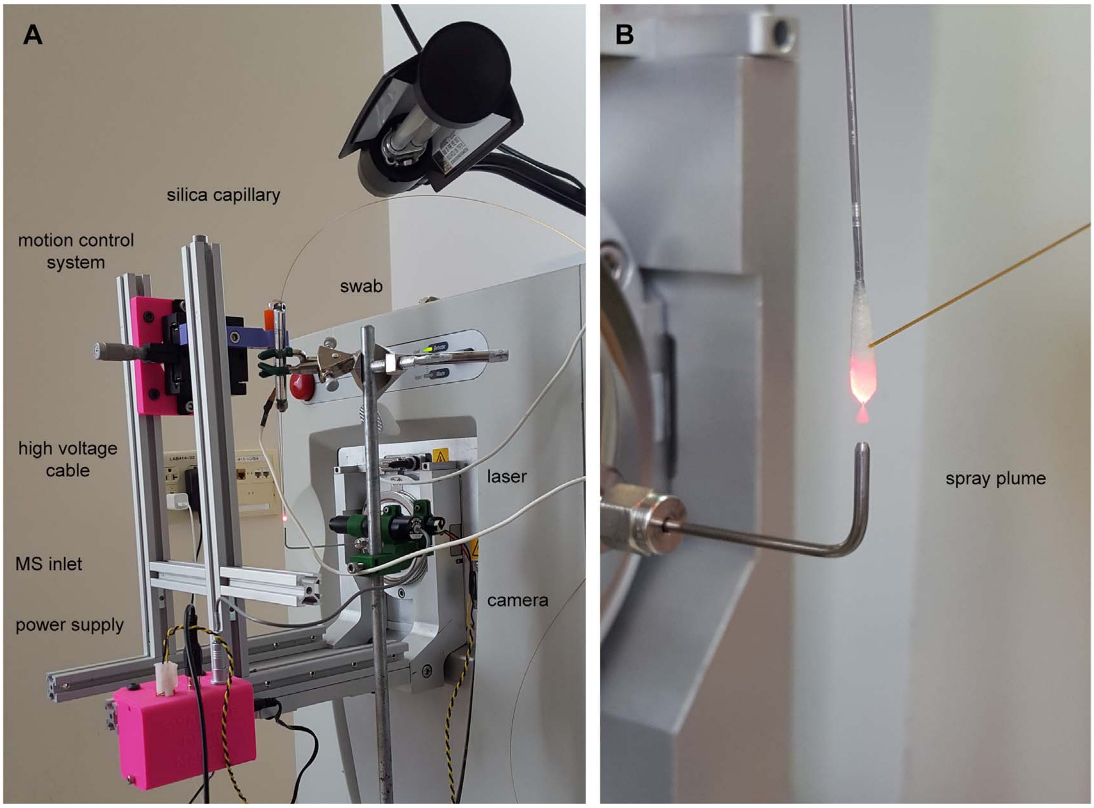

Fig. 1. (A) Image of the custom source interface. **(B)** Photograph of electrospray generated from swab, red laser pointer was used to illuminate the electrospray plume.

illicit drug detection in oral fluid [22], nicotine detection in meconium [24], detection of gunshot residues from human skin [25], detection of chemical warfare agents from surfaces [26]and intraoperative assessment of surgical brain tumor margins [23]. Analyses in the reported methods were qualitative and relied on limits of detection to establish the presence of target analytes (e.g. illicit drugs in biofluids [22]) or relative spectral changes to assess positive outcomes (e.g. presence of cancerous tissue [23]). Swabs were used dry to sample biofluids and tissue in vivo [21,23–25], or conditioned with solvents and then used to sample analytes from dry surfaces [26]. The aforementioned applications used a variety of slightly different methods each of which suggested electrospray ionization behavior. Ionization in STS is believed to occur similarly to that in PS ionization, i.e. ions are generated from a porous surface via electrospray-like mechanisms [12]; however, characterization of ionization behavior in response to operating conditions and details of mechanism in STS have not been studied. With the aim of improving STS performance (i.e. reproducibility of signal generation, signal intensity, and signal stability), we sought to better characterize the parameters which impact ion generation; an aspect of STS that was not discussed in previous articles. In this study, we provide the first visual evidence of electrospray-like behavior in STS and describe the parameters which influence ion generation from commercially-available swabs composed of different materials. Microscopic videography of the spray plume revealed multiple, known, electrospray ionization modes to be present in STS. The parameters which influence STS, the visual observations, and the data are illustrative in this report.

2. Materials and methods

2.1. Medical swabs

Most of the experiments were performed using sterile medical swabs, model 160 C, provided by Copan Diagnostics (Murrieta, CA). The swabs have an aluminum handle and rayon tip of largest diameter of ~ 2.4 mm (Fig. S1). The swabs are packaged in individual tubes for easy transport and storage. They are mounted in a plastic cap that serves as a convenient holder. Each tube and cap assembly is sealed with a tamper proof label for assurance of sterility and chain of custody. Additional swabs manufactured by Puritan Medical Products (Guilford, ME) were also tested, specifically models 25-800 C50, 25-800 R50 (Fig. S1), and 25-801 D50. These swabs have a flexible aluminum handle and a tip made of cotton, rayon, and polyester, respectively. Tips are of fused shape with largest diameter of ~ 1.8 mm. Swabs having an electrostatic dissipative (ESD) plastic handle (model TX750E, Texwipe, Kernersville, NC) were tested (Fig. S1). These swabs have a conical tip in polyurethane with ~ 0.8 mm in diameter at the apex. Lastly, a 10-µL Mitra® microsampler device (Neoteryx, Torrance CA) was tested. This device has a swab tip that allows for accurate and precise collection of biofluids using VAMS™ technology, and a plastic handle. All the swabs tested are commercialized for purposes other than MS analysis. They have been used with no modification from their commercial form.

2.2. Chemicals

Most of the experiments were performed by spraying pure organic solvents -– ranging from hexanes to N,N-dimethylformamide (DMF) – using different swabs and electrospray conditions. Table S1 summarizes all the solvents tested, their surface tension, viscosity, dielectric constant, and density. All solvents were HPLC grade (≥ 99.9% pure) and were purchased from Sigma-Aldrich (Minneapolis, MN). A few binary and ternary mixtures of solvents were also tested (Table S2). Formic acid (LC-MS grade, Fisher Scientific, Belgium) at 0.1% v/v and the non-ionic surfactant octyl β-D-glucopyranoside (≥ 98% pure, Sigma Aldrich) were tested as solvent modifiers.

2.3. Microscopic videography

For each swab tested and each electrospray condition used, videos