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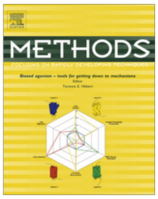

High-repetition rate laser ablation coupled to dielectric barrier discharge postionization for ambient mass spectrometry

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ABSTRACT

Most ambient sample introduction and ionization techniques for native mass spectrometry are highly selective for polar agents. To achieve a more general sensitivity for a wider range of target analytes, a novel laser ablation dielectric barrier discharge (LA DBD) ionization scheme was developed. The approach employs a two-step mechanism with subsequent sample desorption and post-ionization. Effective ablation was achieved by the second harmonic output ($\lambda = 532$ nm) of a diode pumped Nd:YVO_4 laser operating at a high-repetition rate of several kHz and pulse energies below 100 μJ. The ejected analyte-containing aerosol was consecutively vaporized and ionized in the afterglow of a DBD plasma jet. Depending on their proton affinity the superexcited helium species in this afterglow produced analyte ions as protonated and ammoniated species, as well as radical cations. The optimization procedure could corroborate underlying conceptual consideration on the ablation, desorption and ionization mechanisms. A successful detection of a variety of target molecules could be shown from the pharmaceutical ibuprofen, urea, the amino acids L-arginine, L-lysine, the polymer polyethylene glycol, the organometallic compound ferrocene and the technical mixture wild mint oil. For a reliable evaluation of the introduced detection procedure spectra from the naturally abundant alkaloid capsaicin in dried capsicum fruits were recorded.

1. Introduction

Ambient mass spectrometry (MS) has become an indispensable analytical technique for the detection and characterization of organic molecules of different type, composition and size. To enable efficient ion generation, well suited for each component, the development of new ambient ionization techniques has experienced a drastic impetus [1]. A widespread variety of the introduced techniques were employed for direct surface analysis, including desorption and ionization of molecules in a single mechanistic step. Among these single step pick-up and ionization methods the majority relies on already established ionization techniques, such as electrospray ionization (ESI) [2], chemical ionization (APCI) [3], sonic spray ionization (SSI) [4], or photoionization (APPI) [5]. Likewise, the class of plasma-based ionization techniques including, *e.g.*, direct analysis in real-time (DART) [6], flowing atmospheric-pressure afterglow (FAPA) [7], and the dielectric barrier discharge (DBD) [8]/low-temperature plasma (LTP) probe [9], has proven potential for the analysis of compounds directly from untreated surfaces. Plasma-driven ion sources benefit most from their simplicity, flexibility, portability, low power consumption, absence of solvents and offer a high chemical activity. In a comprehensive study Albert et al. demonstrated LTP to be an attractive method for the ionization of low molecular weight compounds over a relatively wide polarity range when compared to conventional ESI and APCI [10].

To address the ionization of less volatile species in plasma-based MS, Martinez-Jarquin et al. [11] investigated the influence of electrode voltage on the plasma temperature in LTP. Adjustment of the plasma properties resulted in an extended applicability towards less volatile analytes, yet not in suitability for low vapor pressure solids. Another approach to increase the analyte population in the surrounding gas phase employs thermal desorption directly out of the bulk, followed by immediate ionization via an individual standalone technique. Nevertheless, this combination was found unsuitable for large molecules and thermolabile compounds such as peptides and proteins [5]. As the applied temperature increased, an increase in signal intensity was observed due to enrichment of analyte in the gas phase, but also the tendency towards unwanted fragmentation processes grew [12]. Each of the above mentioned methods has found important applications in different fields of the life sciences. However, the sensitivity is ultimately limited by combined efficiency of the overall process.

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Since the majority of target molecules is either nonvolatile or thermally labile, an obvious solution to achieve higher sensitivity while maintaining soft ionization is to separate the desorption/volatilization from the ionization processes into two independent steps. Thus, development yielded in different schemes combining laser desorption accompanied by post-ionization.

Providing laser light on the sample surface can enable a well-confined energy input on the sample surface, both spatially and temporally confined. Energy transfer via laser radiation leads to very fast coupling of heat and mechanical stress in the sample. This is followed by an immediate ejection of sample into the surrounding gas phase. In contrast to simple thermal desorption, not only the overall acquisition time can be shortened and a spatially defined interrogation is achieved, but the amount of needed sample volume can be drastically reduced, yielding in similar or in most cases even higher sensitivity [12]. Different combinations have been proposed, including continuous wave lasers and pulsed systems. Especially the application of a pulsed laser can enable gentle desorption of sample matter from the surface, although the laser fluence of pulsed systems is large compared to continuous wave lasers. Soft heating of the sample surface and ultimately volatilization of molecules into the gas phase is obtained due to effective energy dissipation between individual consecutive lasing events. Therefore, the extent of unwanted fragmentation of molecules can be held on a minimum level. Laser ablation produces an abundance of neutral molecules and small particles, while only a minor class of compounds can be directly ionized by exposing them to laser light [13]. Different methods of subsequent ionization of these neutrals already showed promising results.

For ambient chemical imaging applications in case of the above mentioned single-step techniques, lateral resolution is typically low, since sample desorption is commonly delivered by means of a gas flow. Typical values were achieved in the upper μm to mm regime for mapping molecular distributions on the surface, *e.g.* 200 μm for DESI [2], 0.5–1 mm for FAPA [14], 1 mm for DAPPI [5] and LTP [15] and 2–4 mm for DART [16]. In case of DBD and DESI further attempts have been made, minimizing the lateral resolution to a more competitive level with laser-based techniques. Liu et al. constructed a DBD probe which is generating a plasma jet in the 100 μm regime for imaging of cultural heritage [17]. By development of nano DESI Laskin et al. presented MS images with a spatial resolution around 12 μm [18]. In addition, in all fluid-dynamic analyte desorption techniques compounds might be spread to neighboring areas, resulting in a lateral cross talk of individual pixels in imaging experiments.

Until now, the lateral resolution of laser-based systems has not been matched by other ionization techniques for ambient MS. Spatial resolutions of down to a few micrometers and less can nowadays be routinely achieved by commercial instruments. Starting in 1986 Kolaitis and Lubman [19] introduced and pioneered the separation of desorption and ionization of molecules as two individual steps. In their case, a Nd:YAG laser operating at $\lambda = 532$ nm was used to desorb neutrals and ionization was realized via a ^{63}Ni β atmospheric pressure ion source. In 2002 Coon et al. revisited the topic and presented an enhanced system combining laser desorption and chemical ionization via corona discharge [20]. The most popular combination of laser ablation and ESI (LAESI) has been proposed by Nemes et al. [21] in 2007 implementing a mid-IR laser working at 2.94 μm wavelength, but with a comparably low lateral resolution (350–400 μm). This technique is capable of detecting a variety of molecule classes with a mass of up to 66 kDa at low detection limits (fmol). In 2008 Shelley and co-workers [22] were the first to investigate the combination of laser ablation and a plasma-based ionization technique: the FAPA. In their enclosed system, the detectable compounds were limited to a lower mass range of 1 kDa, but the lateral resolution reached 20 μm. In contrast, Galhena et al. [23] reported on an open-air configuration using IR laser ablation metastable-induced chemical ionization (IR-LAMICI) to avoid contamination of enclosure walls. Another tool observing of different types of compounds was based on the irradiation of the ablated sample plume to achieve photoionization of the solvent first and subsequent ionization of sample molecules via gas-phase interactions [24]. More recent publications, however, again refocused on plasma-based strategies as the post-ionization source in combination with continuous wave IR lasers. Both systems, either using a DBD [12] or DART [25] provided enhanced sensitivity compared to the stand-alone technique.

With this contribution, we report on the combination of laser ablation by a pulsed diode pumped solid state laser coupled to a DBD post-ionization probe for ambient MS. Effective ablation is provided by the second harmonic output of a Nd:YVO_4 laser to obtain a wavelength of $\lambda = 532$ nm at repetition rates of several kHz and low pulse energies below 100 μJ. Focusing the laser light ensures ablation on a μm scale while collisions with the excited helium gas stream from the plasma probe effectively ionize compounds with different polarity and vapor pressure. Albeit being efficient for a wide class of analytes, evidence for severe fragmentation processes could not be observed throughout the experiments.

2. Experimental

2.1. Safety

Special care is required throughout when working with high-voltage power supplies. To avoid electric shocks, appropriate safety precautions, such as electrical shielding of the high-voltage lines must be considered. Further safety measures include wearing protective goggles while working with free laser beams. The laser used within these studies is classified as laser safety class 4.

2.2. Chemical reagents

Ultra-high purity helium (99.999%; Linde, Düsseldorf, Germany) was used as discharge gas for the plasma probe. L-Lysine (⩾98%; Sigma Aldrich, Steinheim, Germany), L-arginine (98%; Sigma Aldrich), urea (99%; Acros Organics, Geel, Belgium), polyethylene glycol (PEG) 200 (AppliChem, Darmstadt, Germany) and ferrocene (98%; Acros Organics) were used directly without further purification. The pharmaceuticals ibuprofen and wild mint oil (*Mentha arvensis*, ext.) were purchased from a local pharmacy and dried chilli pepper was obtained from a local supermarket.

2.3. Dielectric barrier discharge probe

Ionization of the ablated material was carried out by a dielectric barrier discharge probe (Fig. 1A). The home-built plasma probe consists entirely of disposable low-cost parts. A high-voltage electrode of copper mesh (1 mm × 1 mm) of 5 mm width was wrapped around the outside of a borosilicate quartz capillary (GB 150-8P, 1.50 mm o.d., 0.86 mm i.d.; Science Products GmbH, Hofheim, Germany). A stainless steel acupuncture needle (NSP 3070 Premium Silver Handle, length: 10 cm; Akupunkturnadeln-Wandrey GmbH, Berlin, Germany) was used inside the capillary as the grounded counter-electrode. A 1/16″ Swagelok tee-piece and Teflon sealing band was used to fix the position of the grounded electrode and the inlet of the discharge gas. The discharge gas streams through the glass tube to facilitate the discharge and to fluid-dynamically support the transmission of analyte ions into the MS inlet. The flow was monitored and adjusted in the range of 0–2.0 L/min by a mass flow controller (GFC17; Analyt-MTC GmbH, Müllheim, Germany).

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