Development and Optimization of an inlet system for Desorption Atmospheric Pressure Photoionization – Mass Spectrometry (DAPPI-MS)

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Introduction

At the 56[th] Annual ASMS Conference on Mass Spectrometry and Allied Topics the Vapur® API Interface was presented [1] and patented in 2010 by Ionsense Inc. (Saugus MA, USA) [2].

The Interface was designed to improve the collection efficiency of desorbed ions generated by ambient pressure desorption ionization sources, such as DART [3]. A factor of 500 increase in sensitivity for the analysis of Verapamil directly from rat plasma and a significant improvement in the overall sample-to-sample reproducibility was reported. The patent holders deem the "jet separator effect" as the physical principle behind the observed progress in sensitivity [2].

This effect allows to efficiently separate the heavier analyte molecules from the lighter carrier gas due to fluid dynamic properties within a jet expansion.

In this contribution a comparable interface was optimized for the application in desorption atmospheric pressure photoionization (DAPPI) [4]. Along the work the proposed working principle was carefully scrutinized.

Methods

MS Xevo Qtof, Waters Corporation, Milford, MA, USA

Ion Source APPI with a Microship Heated Nebulizer (micro-APPI) [5]
100 ml/min nitrogen
3 µl · min^{-1} liquid sampling flow

Radiation Source VUV Kr discharge lamp (Heraeus Noblelight GmbH, Hanau, Gemany)

Analytes Mix 1:
testosterone (1 µM), benzo[a]pyrene (1 µM), 1-naphthol (2 µM), cholesterol (2 µM), creatinine (2 µM), verapamil (2 µM), C12-ceramide (10 µM)

Mix 2:
testosterone (10 µM), benzo[a]pyrene (10 µM), 1-naphthol (10 µM), cholesterol (10 µM), creatinine (10 µM), verapamil (10 µM), C12-ceramide (10 µM)

Vacuum pump Rotary Vane Vacuum Pump TRIVAC type D16B (Leybold Vakuum GmbH, Bonn, Germany)
Capacity: 16 m^3 · h^{-1}

Method - DAPPI

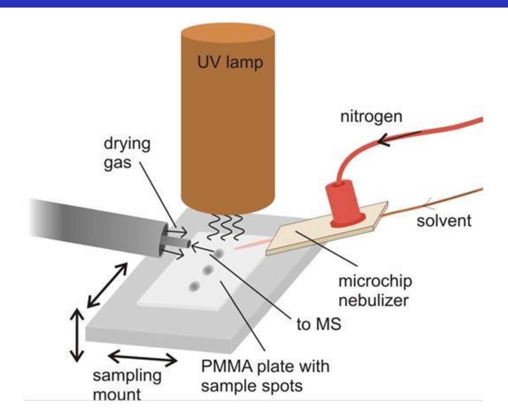


Figure 1: A schematic of the desorption atmospheric pressure photoionization (DAPPI) setup.

- A heated nebulizer microchip sprays a hot plume consisting of nitrogen gas and vaporized solvent
- The hot vapor jet is directed towards the sampling surface
  → Thermal desorption of analytes to gas phase
- A krypton discharge lamp emits 10 eV photons that ionize the solvent
  → gas-phase reactions lead to ionization of the analytes

Inlet System Design

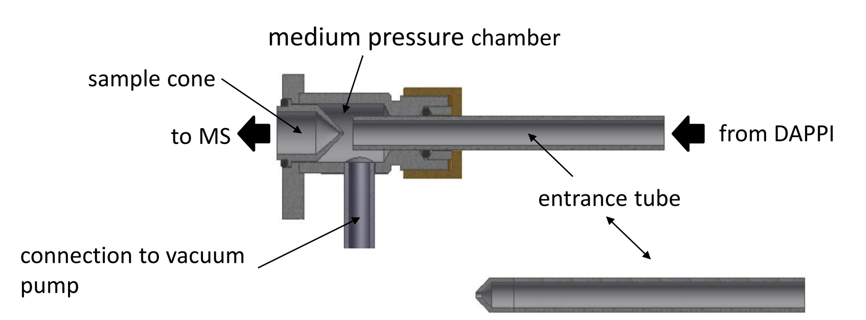


Figure 2: A schematic of the developed DAPPI inlet system

The developed inlet system is designed along the line of the Vapur API interface for Direct Analysis in Real Time (DART) [3]. A vacuum pump connected to the medium pressure chamber maintains an increased, regulated volume flow through an entrance tube. Different entrance tubes (cf. Table 1), for example with a convergent nozzle at the low pressure end of the tube nozzle allowed a directed gas flow onto the MS inlet sample cone. Due to its reduced inner diameter (i.d.) this nozzle enables a choked flow. The gap distance between the entrance tube and the MS inlet sample cone can be varied. For a better ion focusing a potential gradient can be applied between the entrance tube and the sample cone. Additionally the entire interface can be heated.

no.	sample cone: cone i.d. [mm]	choked volume flow* [L·min^{-1}]
1	0.36**	1.2
2	0.5	2.4
3	1.0	9.4

no.	entrance tubes: tube i.d. [mm]	choked volume flow* [L·min^{-1}]
1	1	7.9
2	2	26.2
3	5.1	-

no.	entrance tubes with nozzle: tube i.d. [mm]	nozzle i.d. [mm]	choked volume flow* [L·min^{-1}]
4	2	1	9.4
5	2	1.5	21.2
6	5.1	1	9.4
7	5.1	1.5	21.2

Table 1: Overview of the different entrance tube and MS inlet sample cone geometries.

* Calculated from Ref. [6]; ** original MS inlet sample cone

Experimental Setup

To reduce the set of parameter and to provide a continuous and stable sample introduction, the new interface was characterized and optimized using micro-APPI [5]. For the iterative optimization of the ion transmission, several parameters (listed in section: Inlet System Design) were carefully assessed.

The sample solution was infused with a syringe pump (3 µL·min^{-1}) and nitrogen was used as the microchip nebulizer gas (100 mL·min^{-1}). The microchip was mounted on a xyz-stage, which enabled an exact and reproducible spatial alignment of the assembly. The microchip was further resistively heated with a common DC power supply. Performance improvement of each source development iteration step of the new inlet system was carefully assessed with comparative measurements of a sample mixture containing pharmaceutically relevant substances. Depending on the flow restrictions of the entrance tube and sample cone (cf. Table 1) the connected vacuum pump allowed to maintain background pressures in the interface enclosure ranging from 100 mbar to 1000 mbar. The pumping speed was regulated with a swagelok valve and the pressure is monitored with a commercial barometer.

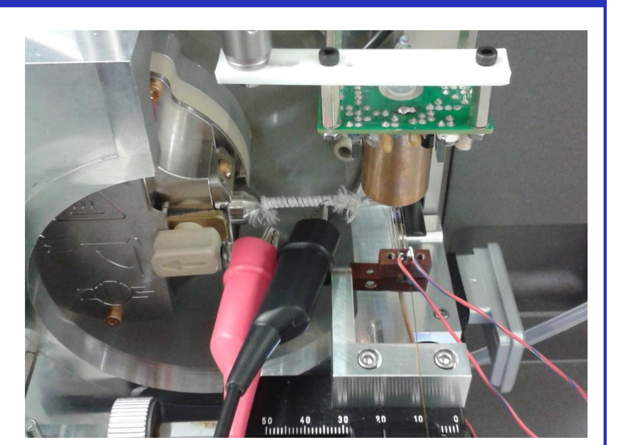


Figure 3: The conventional micro-APPI setup

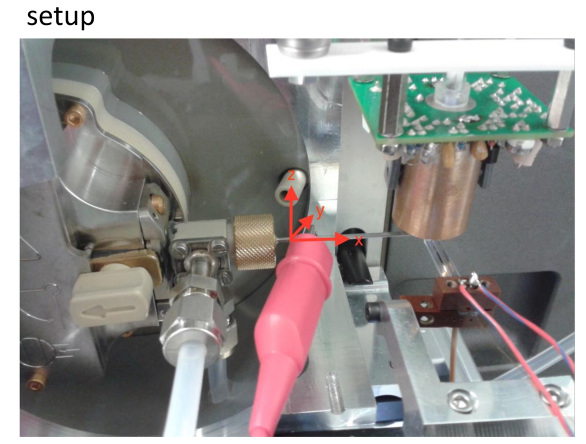


Figure 4: The developed inlet system setup for micro-APPI

Theory and Questions

Due to vacuum restrictions, most LC/MS instruments collect only a small fraction of the desorbing gas (cf. Figure 5, left). Typical volume flows of these instruments range between 1 and 2 L· min^{-1}. Enhancement of the ion collection efficiency from the desorption/ionization region can be achieved by increasing the volume flow of the gas transporting the desorbed analytes.

With an additional differentially pumped stage more of the desorbing gas plume containing analyte ions is collectetd (cf. Figure 5, right)

If the pressure ratio becomes sufficiently high, a free jet under continuum conditions would form (cf. Figure 6). In this case, compounds with high diffusivity would be deflected from the central flow axis (jet separation effect). The diffusivity is proportional to the root of the inverse mass. Thus the lighter background gas would diffuse more than the heavier analyte ions. Consequently, a reduction of the volume flow and an enrichment of the analyte would be achieved.

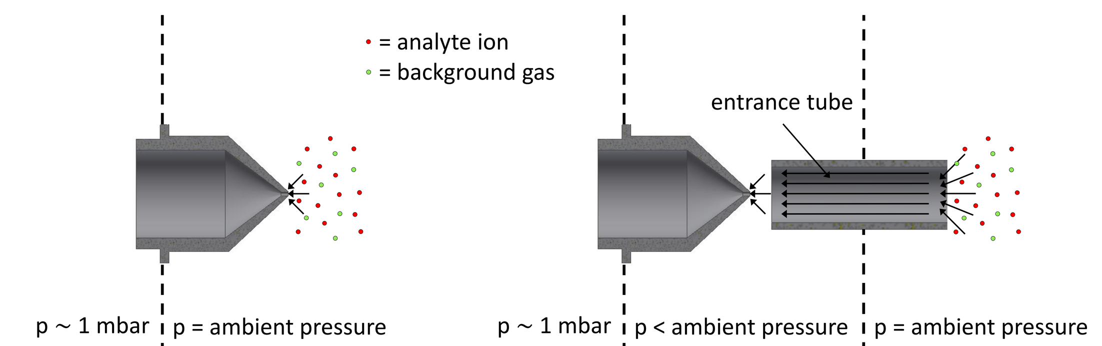


Figure 5: Left: A schematic of the conventional MS inlet sample cone. Right: A schematic of the Vapur API interface.

Boundary Conditions for a free jet expansion under continuum conditions.

For continuum flow characteristics the gas has to be sufficiently dense, as expressed with the Knudsen number K_n:

$$K_n < 0.01 \qquad K_n = \frac{\bar{l}}{d}$$

$\bar{l}$ = Mean free path
d = diameter flow channel

To form a jet, the pressure ratio $\frac{P_0}{P_1}$ has to be > 15 [7]. In this case the position of the mach disk is calculated by:

$$x_m = 0.67 * D_0 * \sqrt{\frac{P_0}{P_1}}$$

x_m = location of mach disk
D_0 = nozzle diameter
P_0 = upstream pressure
P_1 = downstream pressure

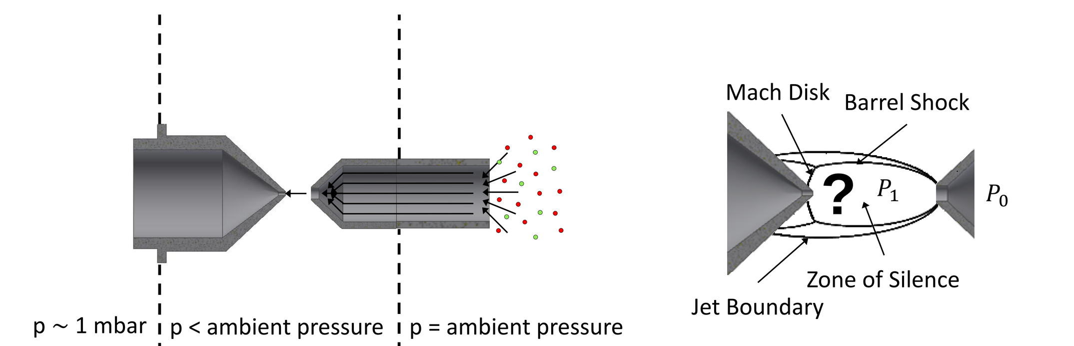
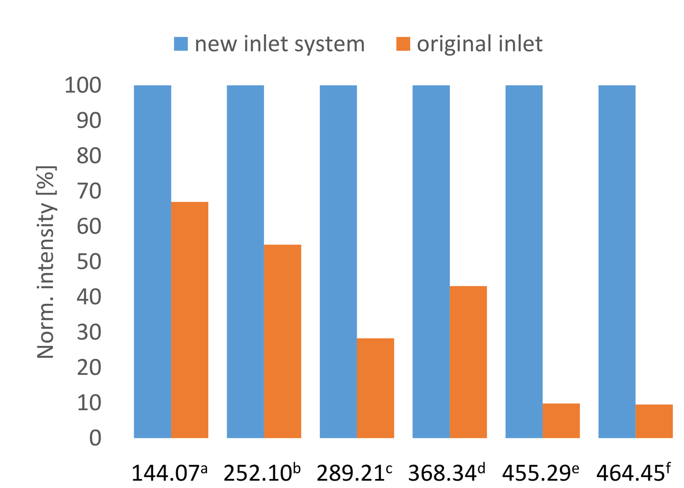


Figure 6: Left: A schematic of the new inlet assembly with a convergent nozzle at the low pressure region. Right: Enlarged section of the gap region and the proposed jet expansion.

For the original Vapur API Interface configuration the estimated total maximum pressure drop is 10 mbar. Accordingly, the pressure ratio is near unity, which renders the jet formation under these conditions unlikely. The observed intensity and stability increase is most probably attributable to a simple improved collection efficiency of the desorbed material.

Results

Figure 7: Comparison between the new inlet system and original inlet. Summed ion signals (1.5 min) of selected analyte masses: [a]1-naphthol (MH$^+$), [b]benzo[a]pyrene (M$^+$), [c]testosterone (MH$^+$), [d]cholesterol ([M-H$_2$O]$^+$), [e]verapamil (MH$^+$), [f]C12-ceramide ([MH-H$_2$O]$^+$)



By successively changing all variable device parameters the new inlet system was characterized and optimized. The optimal observed configuration was entrance tube 7 paired with MS sample cone 2, a reduced pressure within the interface, an applied potential gradient and a gap distance of 2 mm. The comparison between the original setup and the new inlet system demonstrate that the new inlet system improves the transfer and collection efficiency of ions generated in the ionization region (cf. Figure 7). Considering that no electric potential gradient was applied on the new inlet system during the presented comparative measurements due to experimental problems, even better results can be expected.

Mass spectra with the new inlet system show lower background. Furthermore, a comparison of the mass range from m/z = 50 to m/z = 250 indicates discrimination of lower masses with the new inlet system. This trend is also seen in Figure 7. The relative intensity gain increases with higher m/z. The reason for these observations is still under investigation.

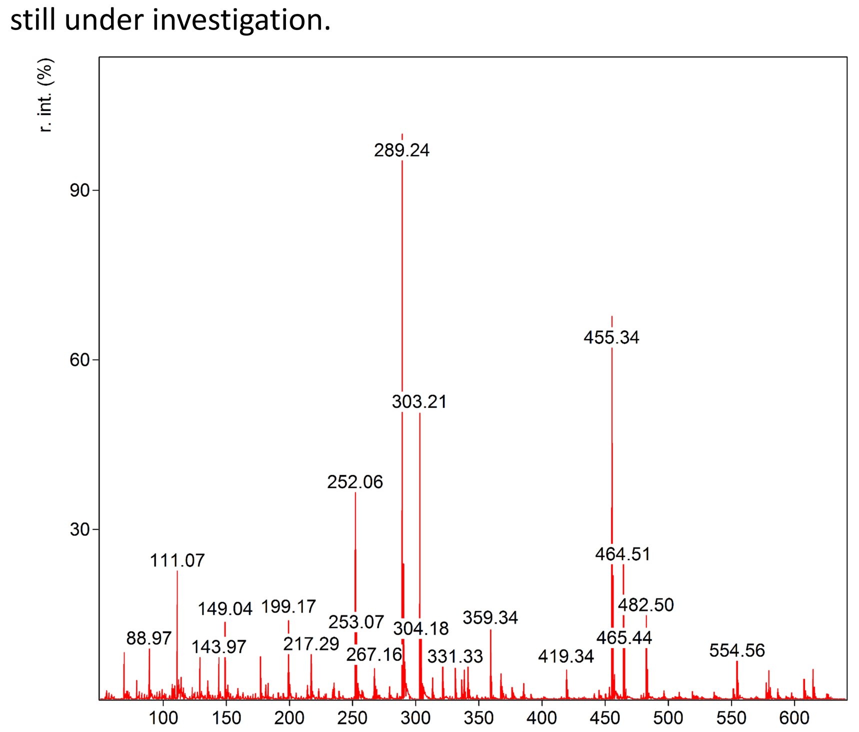
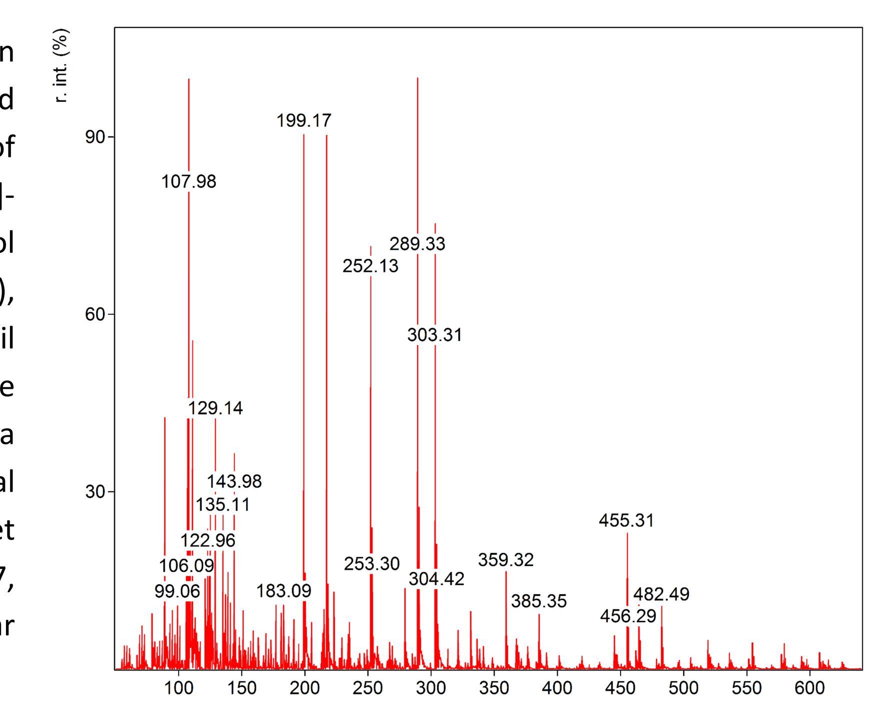


Figure 8: Comparison between the new inlet system and original inlet with a mixture of testosterone (10 µM), benzo[a]pyrene (10 µM), 1-naphthol (10 µM), cholesterol (10 µM), creatinine (10 µM), verapamil (10 µM), C12-ceramide (10 µM). Summed mass spectra (1.5 min). Right: the original setup. Left: the new inlet system. Entrance tube no. 7, interface pressure 400 mbar and gap distance 2 mm.



Conclusions

The systematic variation of the interface parameters has shown that:

- The ion collection efficiency from the desorption/ionization region is increased by an increasing volume flow.
- An applied potential gradient between the entrance tube and the MS inlet sample improved the transfer efficiency.
- The pressure within the medium pressure chamber has a significant impact on the ion collecting and transfer process, depending on the entrance tube geometry and the nebulizer chip position.
- Sufficiently low pressures in the intermediate chamber caused significant changes in the flow dynamics, perceptibly observed in increased ion-molecule clustering.
- Signal intensities are not temperature dependent (28 - 200°C).

The increase in sensitivity is mostly assigned to the improved collection efficiency. **As in general, such a system will be more efficient and less prone to environmental influences the more encapsulated it is designed.** If in fact a jet expansion is responsible for the notable low mass discrimination is questionable and still under investigation.

The introduced inlet geometry is also of interest for ambient laser ablation methods to increase the collection efficiency of ablated plumes. Accordingly, further applications with LAAPI [8] are envisaged.

Literature

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