

Performance Study of an Extended Length Particle Discriminator Interface for Desorption Electrospray Ionization

Gary J. Van Berkel,¹ Vilmos Kertesz,¹ Bradley B. Schneider,² and Thomas R. Covey²
¹Oak Ridge National Laboratory, Oak Ridge, TN and ²MDS SCIEX, Concord, ON, Canada



OVERVIEW

Purpose:
 Evaluate and utilize an extended particle discriminator interface (PDI) for Desorption Electrospray Ionization Mass Spectrometry (DESI-MS)

Methods:
 Signal levels were measured for electrospray (ES) ionization of standard solutions with different length particle discriminator interfaces on an AB/MDS SCIEX 4000 Q TRAP mass spectrometer
 Standard curves for spotted standards on TLC plates and hydrophobic surfaces were obtained
 Chemical images of drugs and metabolites in tissue thin sections were acquired

Results:
 A PDI provides a suitable interface geometry to allow spot sampling, lane scanning, and imaging of chemicals on various surfaces and in tissue thin sections
 ESI signal levels are moderately attenuated as heated chamber length of the PDI increases

INTRODUCTION

Interfacing an atmospheric pressure sampling mass spectrometer with particular ionization sources can be simplified with a capillary like extension out from the mass spectrometer.

The proper positioning of the atmospheric sampling inlet this condition can be met easily. Interfaces that use an orifice and curtain gas require an alternative.

For instrumentation that uses a heated capillary inlet this condition can be met easily. Interfaces that use an orifice and curtain gas require an alternative.

A particle discriminator interface (PDI) provides such an alternative [1,2].

We modified the standard Nanospray® interface (PDI) of a commercial mass spectrometer (AB/MDS SCIEX, 4000 Q TRAP®) with heated chambers of extended length.

We report here on the performance characteristics of the PDI using electrospray (ES) ionization and desorption electrospray ionization (DESI) and demonstrate the ability with the PDI to spot sample and image with DESI.



EXPERIMENTAL

All experiments were performed on an AB/MDS SCIEX 4000 Q TRAP® mass spectrometer (MDS SCIEX, Concord, ON) using a heated Nanospray® interface and particle discriminator interfaces with heated chamber lengths of 2.0, 4.0, 7.0 and 12 cm (Figure 1). Test compounds were prepared in water, methanol, acetonitrile, isopropanol or mixtures thereof. ES – MS/MS (SRM) signal levels were tested by continuous infusion of the standard solutions at 2.5, 5.0, and 10 µL/min in an on-axis position about 1 cm from the entrance of each respective interface.

The DESI sprayer, surface control and automation, and data analysis software have been described in detail elsewhere [4] (see Figure 2 below).

DESI signal levels were measured from samples hand spotted onto normal phase TLC plates or onto a printed teflon surface.

Chemical images of 40 µm thick sagittal whole mouse tissue sections mounted on glass slides were obtained using 80/20 (v/v) acetonitrile/water at 5 µL/min as the DESI spray solvent.

Figure 1. Standard and Modified PDI

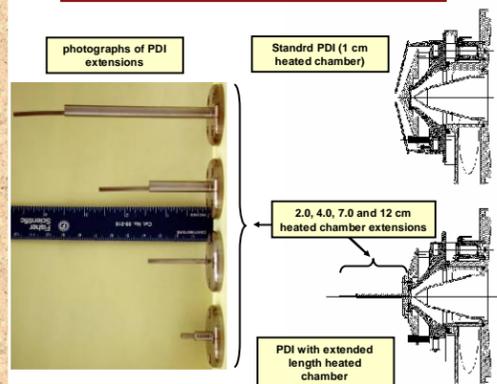
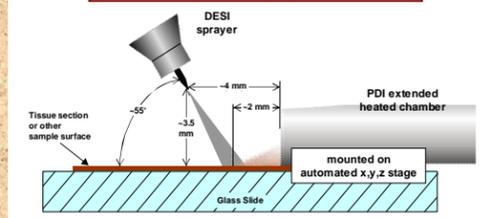


Figure 2. Sampling Geometry for DESI Spot Sampling and Imaging with a PDI



DESI spray emitter was a 5.2 cm long taper-tip fused silica capillary (50 µm i.d., 360 µm o.d., New Objective, Woburn, MA) in a MicroNanospray II (500 µm i.d. nebulizing gas tube. The nebulizer gas flow rate was set to ca. 1.3 L/s (gas 1 = 40; ca. 228 m/s linear velocity). The ES HV (4-5 kV) was applied to the stainless steel body of the MicroNanospray II.

RESULTS AND DISCUSSION

When using the PDI interface with a typical on-axis ES configuration, the SRM signals recorded for reserpine, verapamil, and propranolol, in positive ion mode, showed less than a factor of 5 drop off in signal from the normal nanospray interface (1 cm long heated chamber) up to the 12 cm long heated chamber.

The drop off in signal was more significant in the case of ibuprofen and taurocholic acid which were detected as negative ions

The drop off in the DESI experiment may be less than the ES experiment because of the reduced solvent load into the interface with DESI at the same solvent flow rate. Those experimental measurements are planned.

Figure 3. SRM Signal Levels in ES-MS with Different Interfaces

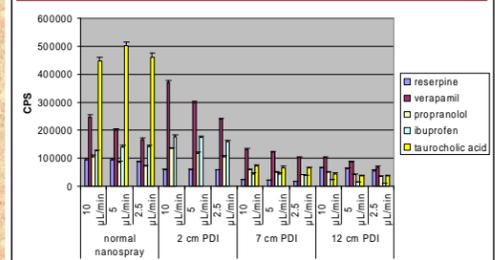
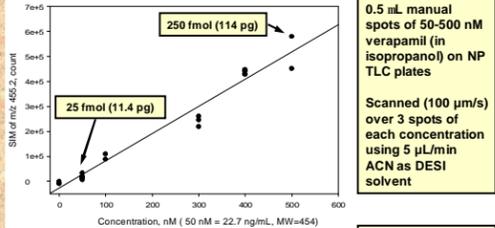


Figure 4. Verapamil SIM Signal Levels in DESI-MS with 12 cm PDI

In DESI, when manually spotted on a normal phase (NP) TLC plate, a linear response curve was obtained for 0.5 µL spots of 50 – 500 nM solutions. The LOD was estimated to be ca. 11 pg (25 fmol).



Best LOD obtained when spotting samples on a hydrophobic Teflon surface that kept the spot size to a minimum. The lowest amount of verapamil detected was from a 0.5 µL spot of a 1 nM (0.45 ng/mL) solution. The LOD estimated to be ca. 227 fg (ca. 0.5 fmol).

The 7.0 and 12 cm long heated chamber, and our current x,y,z computer controlled sample stage (Figure 5), enabled access to the complete area of a whole body mouse tissue section. Using this setup, we obtained images of portions of the complete sections detecting in one case both the parent drug and one of the major metabolites.

Figure 5. Schematic Illustration and Photograph of DESI Tissue Imaging Setup with PDI

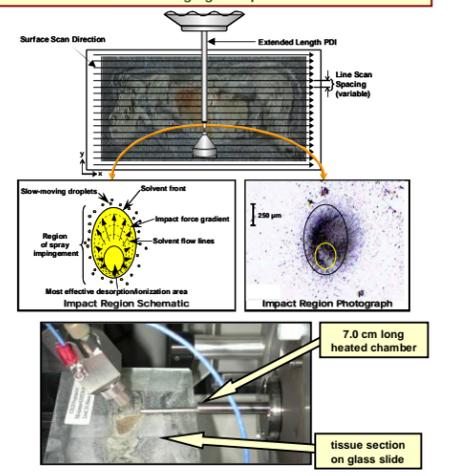


Figure 6. Chemical Image of Tissue Section Revealing Location of Orally Dosed Drug and a Major Metabolite (12 cm heated chamber)

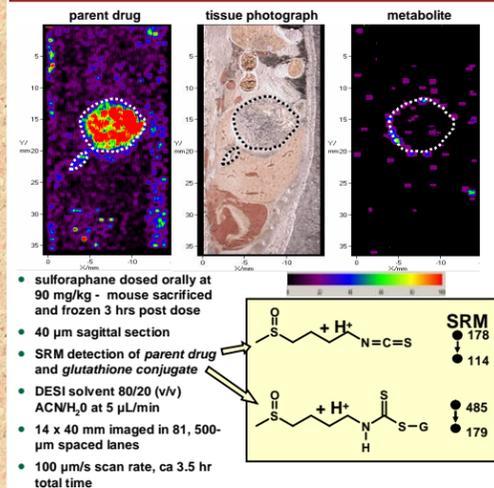
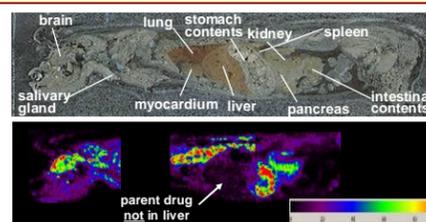


Figure 7. Chemical Image of Tissue Section Revealing Distribution of IV Dosed Drug (7.0 cm heated chamber)



propranolol - IV dose at 7.5 mg/kg
 sacrificed and frozen 20 mins post dose
 40 µm sagittal sections
 SRM detection of parent drug
 DESI solvent 80/20 (v/v) ACN/H₂O at 5 µL/min, 500 µm spaced lanes, 0.1 mm/s scan rate, 3 – 2 cm x 2cm sections imaged (ca 2.5 hrs each – 7.5 hrs total analysis time)

Figure 8. Tissue Levels of Propranolol at 60 min: Comparison of Literature Values and QWBA

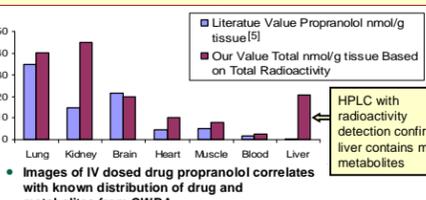
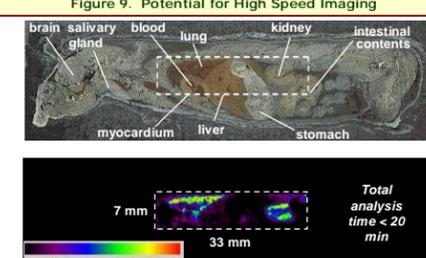


Figure 9. Potential for High Speed Imaging



Same propranolol dosed mouse used in Figure 7 – different section
 SRM detection of parent drug using 30 ms dwell time
 Surface scan rate 0.5 mm/s (5 times faster than in Figure 7)
 ca. 33 x 7 mm section imaged, < 20 min analysis time
 DESI solvent 80/20 (v/v) ACN/H₂O at 5 µL/min, 500 µm spaced lanes

CONCLUSIONS

- A PDI with an extended length heated chamber can be used in place of an orifice and curtain gas arrangement to facilitate the integration of a DESI source for use in spot sampling, lane scanning and chemical imaging of analytes on surfaces
- Signal levels are moderately attenuated as PDI length increases
 - The shortest length PDI practical for the analysis situation will provide the best signal
- With the longest heated chamber used (12 cm), detection levels were as low as ca. 227 fg (ca. 0.5 fmol) for verapamil in SIM mode
 - Detection at these levels was only possible when spotting on a hydrophobic surface that maintained the spot size near the dimensions of the DESI impact plume
 - Detection levels are expected to be improved with shorter PDI extensions and with the use of SRM detection
- DESI-MS/MS (SRM) was successfully used to image the spatial location of parent drug and metabolite in tissue sections from mice dosed orally or by IV at physiologically realistic levels
- Relatively rapid imaging is possible
 - Short dwell times are required so that spatial read out resolution is not compromised

LITERATURE CITED

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