

Charged Droplet Solvent Extraction From Surfaces: Desorption Electrospray Ionization of Small Molecules

Gary A. Valaskovic¹, Mike S. Lee²

¹ New Objective, Inc., Woburn, MA ² Milestone Development Services, Newtown, PA

Introduction

The recent publication (Takats, et al., *Science*, 2004, 306, 471) of desorption electrospray ionization (DESI) demonstrated the ability to generate ESI-like mass spectra for a variety of compounds desorbed from a solid substrate. There are a number of potential mechanisms for ionization, including direct contact of charged droplets with the surface, vapor phase diffusion of analyte into the charged droplet, and ion-molecule reactions. Here, we investigate possible mechanisms for a non-volatile small molecule (drug) analyte deposited directly on smooth, hard surfaces (metal and glass). Our goal is to explore conditions for ionization and compare results from bulk media to those obtained from thin films. Video microscopy of both the ESI plume and substrate correlates MS signal and the physical interaction of the spray plume with the sample substrate.

Methods & Materials

Instrumentation and Components

- Ion trap mass spectrometer (LCQ Deca™, Thermo Electron) fitted with custom capillary tube inlet extender (Figure 1)
- Nanospray Source (PicoView® 500, New Objective) modified to accept a glass or metal sample substrate positioned in front of capillary (Figure 1).
- HPLC Pump (1100 Series, Agilent)
 - Flow 0.25 - 5 $\mu\text{L}/\text{min}$ (50% MeOH, 0.1% Formic Acid)
- Sheath gas-enabled fused-silica emitter (30 μm Tip ID)
 - Sheath gas flow control provided from instrument, velocity varied from 10 to 200 m/sec.
 - Tip position and angle variable

Sample Preparation

A 25 mg/mL solution of buspirone (a basic, anxiolytic drug, Aldrich Chemical) was prepared in water. 10 μL aliquots were deposited onto clean glass or stainless steel substrates and allowed to air dry for > 4 hours. Optical sectioning microscopy revealed the average dried film thickness to be 1 - 2 μm .

A bulk sample of buspirone was prepared by pressing the powder under high pressure in an apparatus similar to an IR pellet press. The bulk sample was measured to be 0.5 mm thick.



Figure 1A (above)
Extended inlet capillary
on the LCQ Deca™
(Thermo Finnigan™)

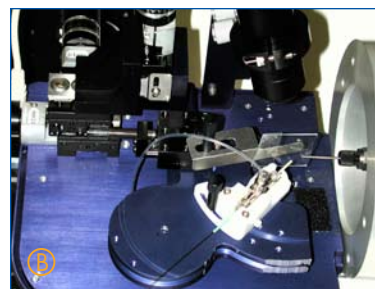


Figure 1B (right)
Modified PicoView®
nanospray source
(New Objective)

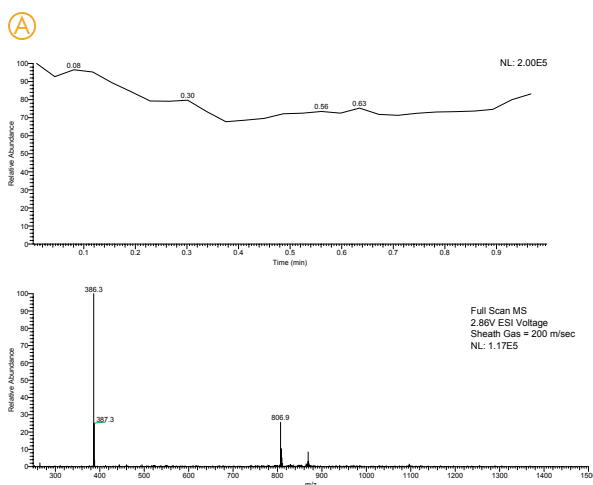


Figure 2A Selected Ion Current (SIC) for the protonated molecular ion of buspirone (386 m/z) for a bulk crystalline sample (0.5 mm thick.) High velocity sheath gas was required for the observation of molecular ion.



Figure 2B Photograph of the sheath gas-assisted electrospray required for DESI analysis. Note the absence of the classic plume-jet spray modality.

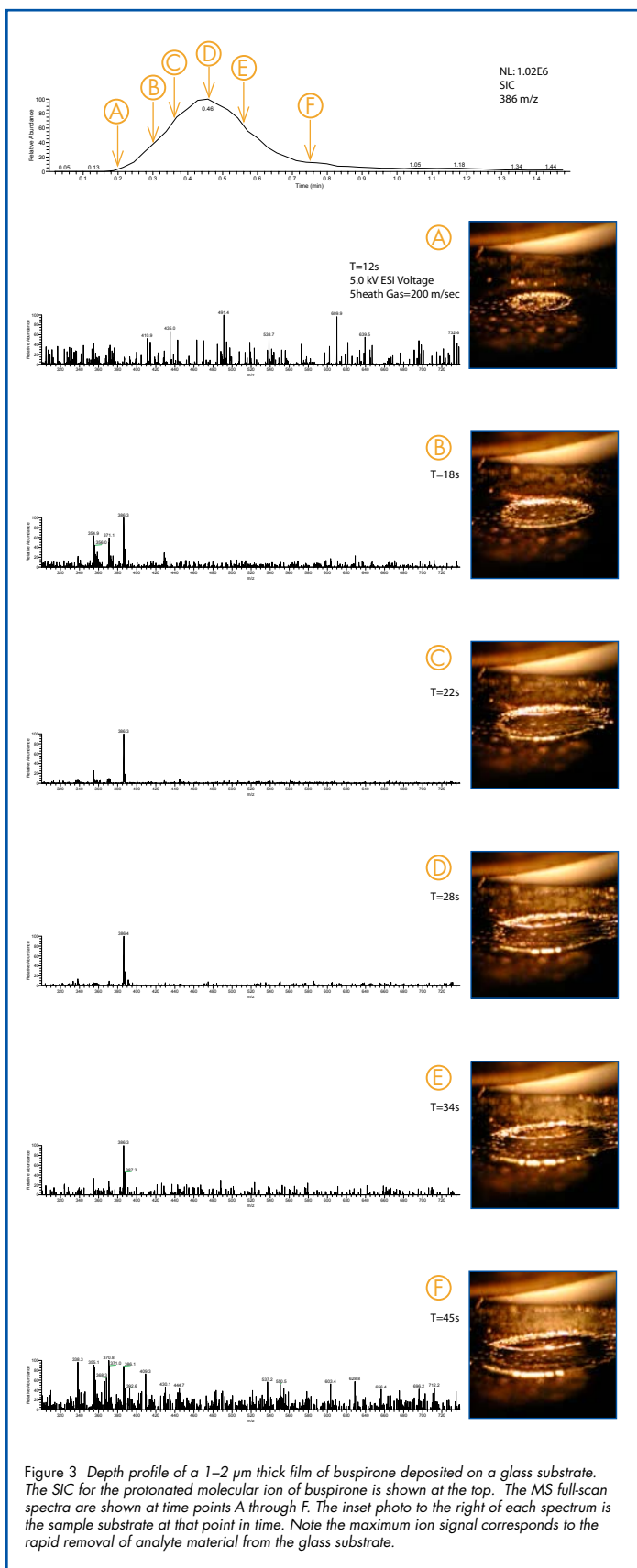


Figure 3 Depth profile of a 1–2 μm thick film of buspirone deposited on a glass substrate. The SIC for the protonated molecular ion of buspirone is shown at the top. The MS full-scan spectra are shown at time points A through F. The inset photo to the right of each spectrum is the sample substrate at that point in time. Note the maximum ion signal corresponds to the rapid removal of analyte material from the glass substrate.

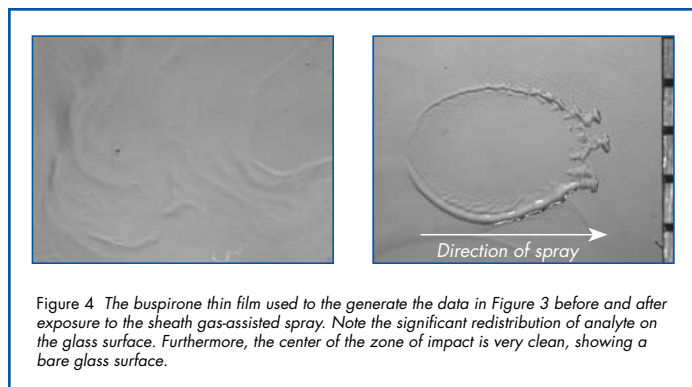


Figure 4 The buspirone thin film used to generate the data in Figure 3 before and after exposure to the sheath gas-assisted spray. Note the significant redistribution of analyte on the glass surface. Furthermore, the center of the zone of impact is very clean, showing a bare glass surface.

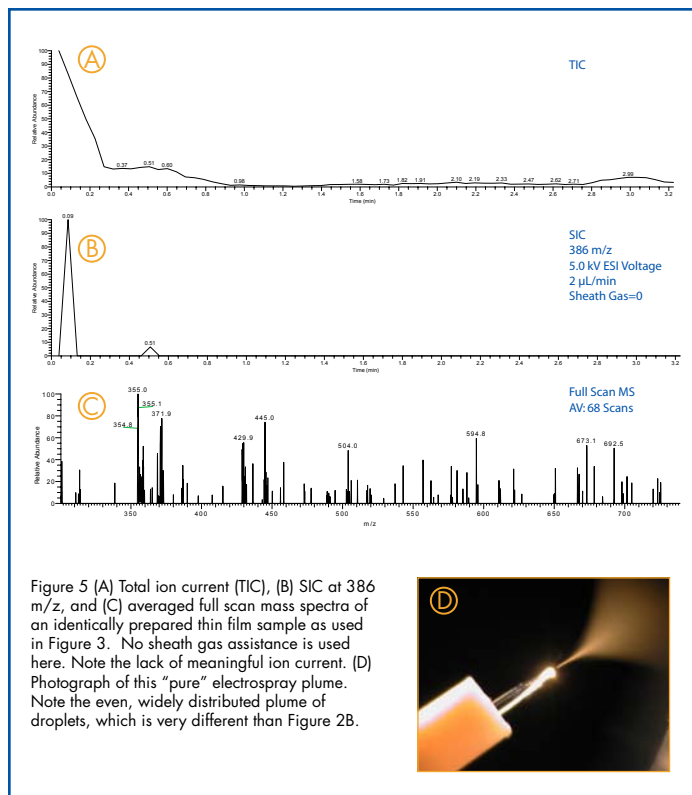


Figure 5 (A) Total ion current (TIC), (B) SIC at 386 m/z, and (C) averaged full scan mass spectra of an identically prepared thin film sample as used in Figure 3. No sheath gas assistance is used here. Note the lack of meaningful ion current. (D) Photograph of this "pure" electrospray plume. Note the even, widely distributed plume of droplets, which is very different than Figure 2B.

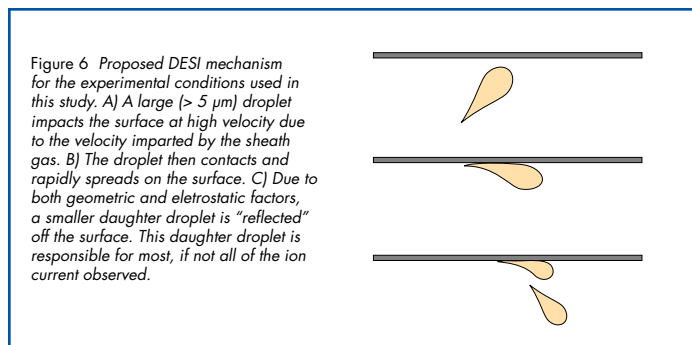


Figure 6 Proposed DESI mechanism for the experimental conditions used in this study. A) A large (> 5 μm) droplet impacts the surface at high velocity due to the velocity imparted by the sheath gas. B) The droplet then contacts and rapidly spreads on the surface. C) Due to both geometric and electrostatic factors, a smaller daughter droplet is "reflected" off the surface. This daughter droplet is responsible for most, if not all, of the ion current observed.

Results

Building on the source geometry described by Takats, et al., the bulk sample was used to optimize spray and MS tuning conditions for the protonated molecular ion of buspirone (386 m/z). Typical results are shown in Figure 2. Signal with the bulk was long lasting (> 30 min.), at which point the experiment was terminated. Microscopic analysis of the substrate after use revealed a large “crater” formation on the surface. No signal was obtainable when the sheath gas flow was reduced to zero, even for a grounded metal substrate.

Observations/Conclusions

The following observations and conclusions were derived from applying DESI to a small molecule thin film on a non-interactive surface.

- DESI can generate very clean spectra of either bulk or thin films for a basic small molecule drug
- Observable levels of ion current require high-velocity sheath gas
- Large amounts of ion current are generated when the sheath-generated plume is capable of a strong interaction with the surface. Such interaction is characterized by high levels of analyte removal and/or redistribution
- No appreciable ion current was observed with a “pure” electrospray plume at 1 $\mu\text{L}/\text{min}$. for either electrically floating glass substrates or electrically grounded metal substrates
- For the analyte/substrate system analyzed, interaction of large ($\approx 1\text{-}10\ \mu\text{m}$) charged droplets with the surface is required for the observation of ion current. This suggests a fraction of these droplets may bounce off the surface or otherwise disintegrate into smaller droplets before entering the vacuum system.