

# Charged Droplet Solvent Extraction from Surfaces: Desorption Electrospray Ionization of Small Drug Molecules

Gary A. Valaskovic<sup>1</sup> and Mike S. Lee<sup>2</sup>

<sup>1</sup>New Objective Inc., Woburn, MA <sup>2</sup>Milestone Development Corp, Newtown, PA

## Introduction:

The recent report (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 small molecule, non-volatile analytes deposited directly on smooth, hard surfaces. Our initial results point to the direct interaction of large ( $\gg 1 \mu\text{m}$ ) charged droplets having a relatively high impact velocity as the dominant mechanism.

## Methods:

The inlet system of a conventional ion trap was fitted with a 5 cm steel capillary extension with a gas-tight connection, providing for duplication of source geometry found in the above reference. A sheath gas (nitrogen) nozzle was constructed from a steel tee. The emitter was fused silica tubing (360  $\mu\text{m}$  OD) with a 30  $\mu\text{m}$  ID nozzle, coaxial in a PEEK sheath tube (0.018" ID). High voltage (3.5 kV typ.) was applied directly to the mobile phase (75% MeOH, 0.1% formic), provided by a capillary HPLC pump (2  $\mu\text{L}/\text{min}$ ), with a platinum wire electrode. An imaging system was capable of imaging either the spray emission or sample substrate during signal acquisition at high magnification.

## Abstract:

10  $\mu\text{L}$  of buspirone (MW 386) at a concentration of 25 mg/ml was deposited either onto a (grounded) polished steel plate, or (floating) glass microscope slide. Dried spot diameter was approx. 5 mm, with a thickness in the micrometer range. Sheath gas flow was varied from zero to 70 (arbitrary units) using the instruments software control. At a sheath gas setting of zero, no significant molecular ion current was observed with either the electrically grounded or floating substrates. This corresponds to conditions of "pure" electrospray, in which highly charged droplets are small ( $< 1 \mu\text{m}$ ). The high quality of the spray plume was directly observable, and in the case of the grounded metal substrate it was indeed attracted to the surface. Little, if any, visible droplet activity could be observed on the surface of the substrate with the microscope. When the sheath gas was raised to a high setting (50-70 arbitrary units) significant molecular ion current was observed, yielding very high quality full scan mass spectra for either substrate. Significant interaction of the droplets with the substrate surface was directly observable through the microscope. It was very clear that large ( $\geq 5 \mu\text{m}$  droplets) were impacting the surface at a high velocity. By the time the signal was exhausted ( $\leq 10 \text{ min}$ ) the majority of the desorbed spot was either removed from the surface of the glass or pushed on the surface to form a crater. Sensitivity with a high sheath gas setting yielded good sensitivity with dried droplets containing as little as 100 fmol of material yielding significant signal for a short period of time ( $\leq 1 \text{ min}$ ). Our current hypothesis is that large, high velocity droplets impact the surface directly, remove soluble analyte from that surface with resulting daughter droplets (free from the surface) yielding spectra.