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Detection and identification of immobilized low-volatility organophosphates by desorption ionization mass spectrometry

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ABSTRACT

Two desorption ionization mass spectrometry (MS) techniques – ultraviolet laser desorption/ionization (LDI) and desorption electrospray ionization (DESI) – have been used to detect and identify low-volatility organophosphates when deposited on surfaces or loaded into the pore volume of porous inorganic or polymeric organic powders. The insecticides malathion and dicrotophos were chosen for this study as simulants of low vapor pressure chemical warfare agents which are inherently difficult to detect directly by traditional methods. Both liquid and powdered forms of either insecticide were readily detected by LDI or DESI MS. LDI MS was performed on a miniaturized home-built time-of-flight (TOF) mass spectrometer and a commercial TOF/TOF instrument. For DESI MS, a home-built ion source was interfaced to a commercial quadrupole ion trap. In LDI, intact molecular ion signatures could be acquired by using an appropriate cationizing agent and powder additive in positive ion mode. Tandem MS was used to confirm the identity of each analyte based on the observed characteristic fragmentation pattern. In DESI, less than 100 pg of the liquid insecticides spotted on clean surfaces were detected, while detection limits for the powder-loaded preparations were lower than 1 μg. The effects of sample surface, salt additives, nanoparticle admixtures, and analyte solubility on the LDI and DESI MS sensitivity have been investigated as well.

1. Introduction

The rapid and confident detection and identification of toxic chemicals is critically important to homeland security, chemical warfare (CW) countermeasures, environmental monitoring, and industrial accident remediation. One key class of toxic analytes is the organophosphate pesticides and nerve agents. Detection of G-class agents with relatively high vapor pressures (e.g., Sarin and Soman) is relatively straightforward by techniques such as ion mobility spectrometry, surface acoustic wave detection, and electron ionization mass spectrometry [1–3]. As the vapor pressure of such toxic materials decreases below $\sim 10^{-4}$ torr (e.g., VX), their detection becomes much more problematic. Detection is further complicated when pesticides or CW agents are immobilized onto organic or inorganic carriers prior to deployment, creating a particulate aerosol that can be inhaled or trapped in small spaces [4,5]. This newer type of potential CW threats requires newer CW sensor methodologies. Such sensor methodologies can also be utilized for analysis of powdered substrates employed as carriers for transport and delivery of pesticides, insecticides, and pharmaceuticals. In addition, rapid response in the case of an industrial accident involving hazardous chemicals also requires the capability to confidently analyze powdered substrates (sand, cement, flour, etc.) for the presence of toxic chemicals.

Conventional CW sensors are based on a variety of detection technologies, including ion mobility spectroscopy (IMS), surface acoustic wave, flame photometric detection (FPD), photoionization detection, mass spectrometry (MS), Fourier transform infrared spectroscopy, etc. [2]. The vast majority of these CW detection devices are configured as vapor detectors and do not easily accommodate low vapor pressure materials that may be dispersed as liquid or dry aerosols. Certain FPD devices are claimed to be effective for aerosol detection, but FPD provides information only for the elemental constituents (e.g., phosphorous, sulfur), and is not specific to individual compounds. Heated inlet systems for IMS, MS, and gas-chromatography/MS instruments have been designed to avoid condensation and facilitate desorption of low vapor pressure analytes, but these systems only provide limited success. A number of desorption/ionization techniques have been developed over the years for the MS analysis of non-volatile molecules, predominantly peptides and proteins. Among those are a variety of LDI techniques [6,7] or particle impact-induced desorption/ionization

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[8]. Recently, DESI (and a host of related ambient ionization methods; see [9] and references therein) has emerged as a powerful tool for studying condensed-phase analytes.

LDI has been traditionally used for the MS detection and structural characterization of low mass non-volatile compounds (synthetic as well as natural products) for more than three decades [10–13]. Several papers describe LDI MS-based detection of environmental contaminants (including pesticides) either from surfaces [14] or adsorbed as residues on individual particles [15,16]. Recently, individual particle LDI TOF MS was applied to detection of CW simulants in micro-sized droplets, aerosolized from liquids [17].

DESI is a versatile atmospheric pressure ionization technique for the rapid *in situ* MS detection of condensed-phase analytes [18,19]. In contrast to LDI, DESI has been developed fairly recently. DESI employs a high-velocity jet of electrosprayed droplets directed toward a sample deposited on a surface placed proximal to the capillary inlet of a mass spectrometer. These droplets impact the sample and cause the analyte to be desorbed from the surface, ionized, and transferred into the mass spectrometer for detection. While the mechanisms of DESI remain the topic of current investigations [9,18–20], this ionization method provides for fast, direct analysis of samples at atmospheric pressure without the need for complex sample cleanup or preparation. Recently, DESI has been successfully interfaced to a miniature rectilinear ion trap MS for possible field applications [21]. DESI has been used previously to analyze a wide variety of substances: pharmaceuticals [18,22–24], illicit drugs [25–28], explosives [18,29–32], polymers [33,34], peptides/proteins [18,35–37], microorganisms [38], and tissue samples [39,40]. Recent work has shown that DESI MS is also useful for the sensitive detection of CW agents, simulants, and their hydrolysis products [31,41–43]. However, these studies investigated only the relatively high-volatility CW simulants and agents, such as DMMP and G-series nerve agents (vapor pressure >0.04 torr), and did not determine the effect of immobilizing the analytes on powdered substrates.

Here we report data from the evaluation of two desorption/ionization techniques – ultraviolet (UV) LDI and DESI – for the rapid MS analysis and identification of low-volatility organophosphate pesticides when deposited on surfaces or loaded into the pore volume of porous inorganic or polymeric organic powders. We note that detection by either LDI or DESI MS of liquid organophosphate analytes loaded into the pore volume of solid particles, such that the powder remains free flowing and non-agglomerated, has not been demonstrated so far. Related studies have utilized secondary ion mass spectrometry [44,45] or single-particle aerosol time-of-flight (TOF) MS [16] to detect the nerve agent VX, the blister agent HD, or pesticides, adsorbed onto the surface of soil particles. Previously, DESI has been applied to detect analytes separated by silica-based thin layer chromatography (TLC) [46,47], which may be related to the silica powder immobilizing substrate employed in these studies. However, effects of the silica plate binder (often an organic polymer or calcium sulfate) and mobile phase salt (ammonium acetate) on DESI from such particle-containing TLC substrates is not known. Additionally, the exact loadings of analyte to particulate are more difficult to evaluate in the TLC studies than in the current work.

2. Experimental

2.1. Materials

Malathion (99% purity; MW_{mono} 330.0 Da; vapor pressure at 25 °C 3.4×10^{-6} torr) and dicrotophos (99% purity; MW_{mono} 237.1 Da; vapor pressure at 25 °C 1.6×10^{-4} torr) were obtained from Chem Service (West Chester, PA) and used without further purification. These were diluted as required for MS analysis (see below for details). Hydrophobic, food-grade modified silicon dioxide powder (Hi-Sil H303, 25 μm median particle size) was kindly provided by PPG Industries Inc. (Pittsburgh, PA). Diatomaceous earth (Celite 521, 3.5 μm median particle size), and alumina (activity grade I, type WN-6, neutral, ~50–200 μm particles) were obtained from Sigma–Aldrich (St. Louis, MO). Polyethylene powder (<20 μm particle size) was purchased from Micro Powders Inc. (Tarrytown, NY). Additional immobilizing agents, including talcum powder and cornstarch (particle sizes unknown) were obtained from local food markets and used without purification. In addition, an insecticide rose dust (Bonide brand) containing 3.00% malathion by weight in an unspecified inert background was purchased from a local garden supply store and analyzed directly. High-purity solvents were purchased from Sigma–Aldrich. 30 nm Si particles (Meliorum Technologies, Rochester, NY) were washed with acetonitrile and resuspended in acetonitrile for a final concentration of ~2 mg/mL.

2.2. Immobilized organophosphate preparation

Dicrotophos or malathion was immobilized on each of the powdered substrates by combining the appropriate amount of pesticide dissolved in methylene chloride with each immobilizing agent in a 50 mL round-bottom flask. In general, three different concentrations of pesticide in each immobilizing agent were prepared: approximately 10%, 1%, and 0.1% by weight (exact concentrations specified in the text). This mixture was stirred for 30 min. The solvent was evaporated using a rotovap equipped with a glass–wool-packed adapter to minimize migration of the immobilized pesticide. The resulting solid was placed under vacuum (0.1 torr) using a glass–wool-packed adapter for 90 min to remove residual solvent. Immobilized preparations were stored in air-tight containers until analysis.

2.3. LDI mass spectrometry

A home-built miniaturized reflectron TOF instrument [48] or a commercial TOF/TOF instrument (Autoflex, Bruker Daltonics, Billerica, MA) were used to acquire spectra in positive ion mode using a N_2 laser at 337 nm. The typical accelerating voltages for each instrument were 10 or 20 kV, respectively, and delayed extraction (~100 ns delay time) was used in the commercial instrument. For tandem TOF/TOF MS, ions were first extracted at 6 kV in the first leg of the instrument. The respective precursor ion and the fragment ions were then selected (isolated) in an ion gate, before re-acceleration in the second (reflectron) leg to 23 keV total energy for a singly charged precursor ion [49]. From several tens to several hundred single laser shot traces were summed for each MS or MS/MS spectrum. Standard commercial (Bruker Daltonics) or in-house written (for the home-built instrument) software was used for post-acquisition MS data analysis. CsI cluster ions were used for calibration up to m/z 1000. Samples for LDI MS were deposited on metal (Al or steel) substrates either neat or mixed with the Si nanoparticle solution and a saturated NaCl solution in ethanol (2:2:1 sample:Si:NaCl, by volume) and allowed to air dry.

2.4. DESI mass spectrometry

DESI MS and MS/MS data were acquired on a Thermo Finnigan LCQ Deca XP Plus quadrupole ion trap mass spectrometer interfaced to a home-built DESI source. The DESI source was essentially