

## Direct analysis of drugs and their metabolites by infrared atmospheric pressure matrix-assisted laser desorption ionization mass spectrometry

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Mass spectrometry is a well established tool for the analysis of the pharmaceuticals and their metabolites. Many of the traditional ion sources, however, slow down the analysis due to the need for extensive sample preparation.

Infrared (IR) atmospheric pressure (AP) matrix-assisted laser desorption ionization (MALDI) mass spectrometry (MS) was successfully applied to the rapid and direct detection of formulated drugs and their metabolites in unprocessed urine. A Q-TOF Premier (Waters Co.) mass spectrometer was modified by replacing the electrospray source with a custom made AP-MALDI interface. To improve the ion collection efficiency, the ions produced by a Nd:YAG laser-driven optical parametric oscillator (running at 2.94 micrometer) were sampled into the mass spectrometer using pulsed dynamic focusing.

A common generic cough medicine formulated as gelatin capsule was cut open for analysis. The active ingredients were acetaminophen, dextromethorphan, guaifenesin and pseudoephedrine. A few microliters of the unprocessed drug and the urine collected at different times after drug ingestion were analyzed directly without drying, extraction or any other preparation steps. Molecular ions and some fragments of all the active ingredients and an inactive ingredient, PEG, were detected in the direct MS analysis of the drug. The urine sample taken after 2.5 hours showed the presence of pseudoephedrine, acetaminophen and PEG. Structural identification of the individual ions, e.g., the protonated pseudoephedrine in urine, was obtained by MS/MS. The dried urine sample did not give any signal, thus its urea content could be excluded as a matrix. The mass spectra obtained after re-wetting the sample spot with water was similar to the original urine mass spectra. This indicated that water played an important role, perhaps as a matrix, in the IR laser desorption ionization process.

Compared to the sample collected at 2.5 hours, the relative ion intensity of pseudoephedrine significantly decreased in the urine taken 24 hours after medication. Thus IR-AP-MALDI mass spectrometry has potential applications in the rapid semi-quantitative analysis of drugs and their metabolites as well as in pharmacokinetics investigations.