Laser and electrospray team up for novel source

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The proliferation of ambient, open-air ionisation techniques for mass spectrometry continues unabated, with the announcement of a unique method designed especially for the analysis of medical and biological samples containing water. It has been dubbed laser ablation with electrospray ionisation (LAESI) and employs the novel combination of an infrared laser with an electrospray to produce ions from solid or liquid surfaces.

The technique has been developed by Akos Vertes and Peter Nemes at George Washington University in Washington, DC. A mid-IR laser is directed onto the target to produce a plume of neutral species and particulates by ablation, the water in the sample coupling the laser energy to the target through the strong O-H absorption band. The plume rises above the target and is intercepted by an electrospray, typically formed from 50% aqueous methanol containing 0.1% acetic acid. The ions in the spray post-ionise the species in the ablated plume and they are drawn into the mass spectrometer.

The ion signal is greater when the electrospray is operated in the cone-jet regime, rather than the pulsating regime. The interaction between the plume and the spray was confirmed by flash shadowgraphy using a fast digital camera equipped with a long distance microscope. The images revealed that the pulsating regime produced larger droplets and a lower duty cycle. The cone-jet regime generated droplets continuously, some being so small that their images were not resolved.

Vertes proposed that the ionisation mechanism involved "the fusion of laser ablated nanoparticles and larger particulates with the charged electrospray droplets. The fused droplets are thus seeded with the analytes from the target, retain their charge, and continue their trajectory towards the mass spectrometer." This mechanism is different to that thought to be occurring in desorption electrospray ionisation (DESI), electrospray laser desorption ionisation (ELDI)

and atmospheric pressure IR MALDI.

The performance of LAESI was demonstrated with the analysis of solutions containing the drugs verapamil and reserpine, for which detection limits of 8 and 25 fmol, respectively, were achieved. The abundances of the protonated molecular ions were linear over four orders of magnitude.

In another test, a healthy volunteer was given a tablet containing the antihistamine fexofenadine and urine was collected for the direct detection of the drug with no sample preparation or pretreatment. The mass spectrum revealed the presence of the drug as well as several, as yet unidentified, metabolites and some endogenous metabolites. Analysis time consisted of spotting the urine onto the sample plate (5 s) and spectrum integration (1 s/sample). In clinical labs, high throughput using well plates and robotics would reduce the spotting time even further.

The analysis of whole blood can be difficult due to the complex mixture of substances present but LAESI revealed several species below 1000 Da. Accurate mass measurements using an orthogonal acceleration time of flight instrument combined with a human metabolome database revealed peaks due to phosphocholine, glycerophosphocholines and haem. At higher m/z values, peaks corresponding to the haemoglobin chains were also observed.

Similarly, the spectrum of lyophilised human serum, which had been depleted of the abundant immunoglobulins, revealed several metabolites as well as a range of multiply charged ions corresponding to human serum albumin.

The high ionisation efficiency of LAESI also permits the analysis of delicate samples with minimal or no injury. Small seedlings of French marigold were placed intact on the target plate and the leaf, stem and root were analysed separately with a single laser shot to minimise tissue damage. Many plant metabolites were detected and identified using a plant metabolome database and some were found to be specific to the area of the plant analysed. The laser damage was limited to small ablation marks which had no effect on the life cycle of the seedlings.

Although the technique looks very promising, and out-performs the related technique of AP-MALDI, the researchers stress the main limitation of LAESI - the sample must have inherent water content. This allows the use of low laser fluences for soft ablation. Tissues such as bone and teeth would require much larger fluences. However, varying the laser wavelength to other absorption bands (such as C-H or N-H) would facilitate their analysis.

Vertes and Nemes pointed out several clear areas for improvement. Directional confinement of the ablated plume would increase overlap with the electrospray and improve ion yield. Increasing the laser fluence would facilitate analysis at larger depths and allow three-dimensional spatial profiling. Size reduction of the

laser spot on the sample could lead to sub-cellular analysis.

Nevertheless, this fledgling ionisation technique has great potential for the analysis of biological and medical samples, as well as delicate living tissue, with the prospect of being extended to in vivo studies.

Related links:

- **W.M. Keck Institute for Proteomics Technology and Applications**
- **Vertes home page**
- ***Analytical Chemistry* 2007, 79, 8098-8106**: "Laser ablation electrospray ionization for atmospheric pressure, in vivo, and imaging mass spectrometry"

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