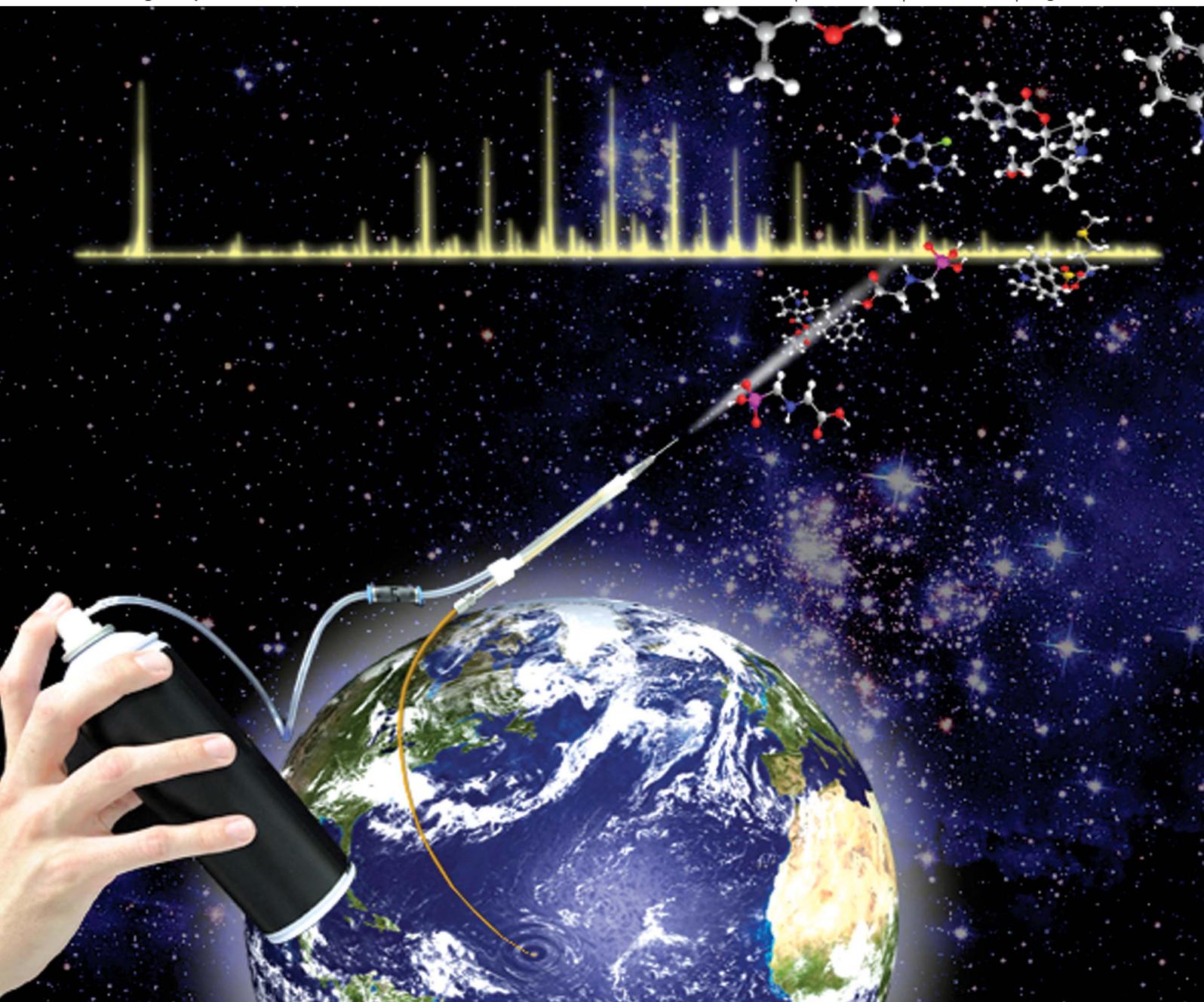


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Easy dual-mode ambient mass spectrometry with Venturi self-pumping, canned air, disposable parts and voltage-free sonic-spray ionization

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An exceptionally easy to assemble source for ambient mass spectrometry is described. Based on Venturi easy ambient sonic-spray ionization (V-EASI), the source was further simplified by the use of a can of compressed air which simultaneously provides solution or solvent Venturi self-pumping and continuous, stable and abundant low-noise ion signal via voltage-free sonic-spraying. Further simplification was also attained by the use of inexpensive and readily commercially available parts: a surgical 2-way catheter, an aerosol can of compressed air, a 30 cm long fused-silica capillary and a hypodermic needle. This “Spartan” V-EASI source seems to offer one of the easiest and cheapest ways to make ions for ambient desorption/ionization mass spectrometry analysis of both liquid and solid samples.

Ambient mass spectrometry¹ has, as one of its key promises, the delivery of a simple platform in which to perform fast and direct MS analysis. Ideally therefore, ambient MS should employ no pre-separation or sample preparation protocols. Simplicity *via* “Spartan” (simple, economical and/or austere) source designs, ideally with no power supplies, auxiliary gases or electrical parts such as pumps or laser or UV light sources or glow discharge devices, is desirable to reduce size, costs, and hence to simplify manufacturing and operation. This simplicity should also benefit general use and service by non-experts (medical doctors and soldiers, for instance) and coupling to portable mass spectrometers.² Recently, we introduced one of the simplest and most economical ionization techniques for ambient mass spectrometry, namely, easy ambient sonic-spray ionization (EASI)³ and have demonstrated its efficacy in a wide range of applications⁴ as a soft, low noise, reproducible, and sensitive (high signal to noise ratio) technique inherently free of electrical, or discharge interferences. EASI uses no heating, no voltages, no lasers and no corona discharges and is solely based on sonic spray ionization,⁵ which produces, when assisted by a cylinder of compressed N₂, a super-sonic stream of very minute bipolar charged droplets of the solvent, which are used to bombard the sample surface. Later, we

introduced a further simplified version of EASI, namely Venturi-EASI (V-EASI),⁶ which incorporated Venturi self-pumping therefore eliminating the need of electrical pumping. V-EASI was also shown to be able to handle both solid (V_S-EASI) and liquid samples (V_L-EASI). V-EASI was also recently applied to wood characterization *via* phytochemical markers⁷ and real time brain tissue analysis.⁸ Herein we describe a further simplified, fully portable version of V-EASI that now eliminates the need of laboratory gas cylinders and regulators, using even simpler parts. This source, we argue, seems to be one of the easiest to assemble and use, most economical yet effective and versatile platforms for ambient desorption/ionization mass spectrometry analysis of both solid and liquid samples.

Experimental methods

Chemicals

HPLC-grade methanol, formic acid and ammonium hydroxide were purchased from Burdick & Jackson (Honeywell), Acros, and Fluka, respectively. Glyphosate (*N*-(phosphonomethyl)glycine) was obtained from Sigma-Aldrich (Steinheim, Germany). The cocaine standard was obtained from Radian (Austin, TX), and PEG 600 was available in our laboratory from a local producer. The synthetic peptide sample (SIS[pT]RK[pY]SPE) was obtained from Proteimax Biotechnology Ltd. Commercial tablets of sildenafil and acetylsalicylic acid were purchased in a local drugstore.

Mass spectrometry

All the experiments were performed in a HCT Ultra Mass Spectrometer (Bruker Daltonics) which had its ESI source removed. Mass spectra were acquired over the 50–2000 *m/z* range.

Results and discussion

Fig. 1 shows both a schematic of the Spartan V-EASI source, which was built using simple and readily commercially available parts, and an actual picture of the system in operation. A surgical 2-way catheter functions as the T-connector. An aerosol dust cleaner can of compressed air (Implastec Co.) was used in replacement of the compressed N₂ cylinders and gas regulators,⁹ and was connected to one of the channels of the 2-way catheter. A 30 cm long fused-silica

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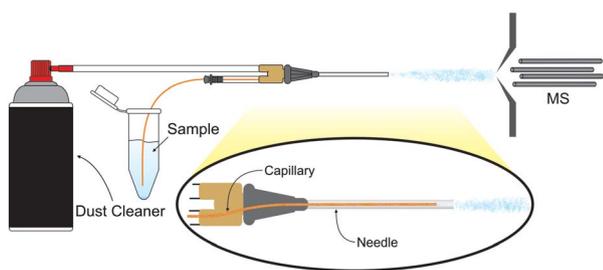


Fig. 1 A schematic and an actual view of the Spartan V-EASI source.

capillary (i.d. 100 μm , o.d. 373 μm) was introduced by the other channel of the T-connector. A simple hypodermic needle (o.d. 410 μm) was then connected to one of the catheter ends, allowing the silica capillary to pass through its steal capillary. The end of the silica capillary was positioned few millimetres (*ca.* 3–4 mm) before the tip end of the needle, in order to simultaneously generate proper self-pumping *via* the Venturi effect and sonic spraying. Pneumatic tube fitting was used for sealing. For liquid samples, V_L -EASI, the other end of the capillary was dipped in the analyte solution; for solid samples, V_S -EASI, methanol was used as the spray solvent and the tip of the hypodermic needle was manually positioned close (*ca.* 5 cm) to the MS orifice in a nearly perpendicular orientation. For V_L -EASI, an angle of *ca.* 40° was used, as previously described.⁶

Despite the simplicity of this Spartan EASI apparatus, the simultaneous self-pumping and sonic spray ionization could both be efficiently attained by the quite constant gas flow provided by the dust cleaner can. Such cans contain compressed air and use hydro-chlorofluorocarbons (HCFCs) as propellant. Since no voltages are applied to promote V-EASI, the air/HCFC mixture was found to produce no chemical interferences at all in the V-EASI(+) or V-EASI(–) mass spectra. Although the generated gas flow is dependent on the force manually applied to the valve can, pressing the valve all the way down produced a nearly constant gas flow of 4.0 L min^{-1} that could be sustained for 2 min with *ca.* 5 min of rest, for a total of *ca.* 40 min of MS acquisition. Periods of use longer than 2 min cause excessive cooling of the can leading to decreased gas flows. A few seconds of spraying is normally sufficient to produce a proper V-EASI mass spectrum. In general, efficient and constant spraying was attained up to 95% of can consumption. In the laboratory or in the field, the can could be easily replaced providing nearly continuous use of the Spartan V-EASI source. For Venturi self-pumping, a solvent (or analyte solution) flow rate of *ca.* 300 $\mu\text{L min}^{-1}$ was attained in our prototype system (Fig. 1) using the commercially available parts, but we believe that lower solvent flow rates could be achieved by further system optimization. The internal/external

diameters of the fused silica capillary as well as the internal diameter of the needle are crucial to obtain proper Venturi effect and adequate sonic spraying. Small changes in these parameters could either eliminate the Venturi effect or degrade the spray conditions causing, for instance, solvent dipping at the needle end reducing ion abundances and causing high consumption of the solvent/analyte solution.

After major parameters were optimized for the Spartan V-EASI prototype model, and sonic spraying and Venturi self-pumping were properly obtained, we ran some classical ambient MS samples to be able to compare the ionization efficiency of such a simple device. Fig. 2A shows the V_L -EASI(+) mass spectrum for an acidified methanolic solution of cocaine (25 ng mL^{-1}). The protonated molecule of cocaine of m/z 304 was observed as the major, very abundant ion and, as previously observed for the archetype V_L -EASI source,⁶ no dimmers, fragments or adducts are detected. Note also the very reduced level of solvent noise. Fig. 2B shows the V_L -EASI(+)-MS for an aqueous solution of a synthetic peptide (100 $\mu\text{g mL}^{-1}$). Note again the similar performance for aqueous solutions of biomolecules as compared to the archetype V_L -EASI source,¹⁵ and the detection of $[M + H]^+$ and $[M + 2H]^{2+}$ ions of m/z 1327.5 and 664.2, respectively. Fig. 2C shows the V_L -EASI(–)-MS spectrum of a methanolic solution spiked with NH_4OH of the herbicide glyphosate (50 $\mu\text{g mL}^{-1}$)

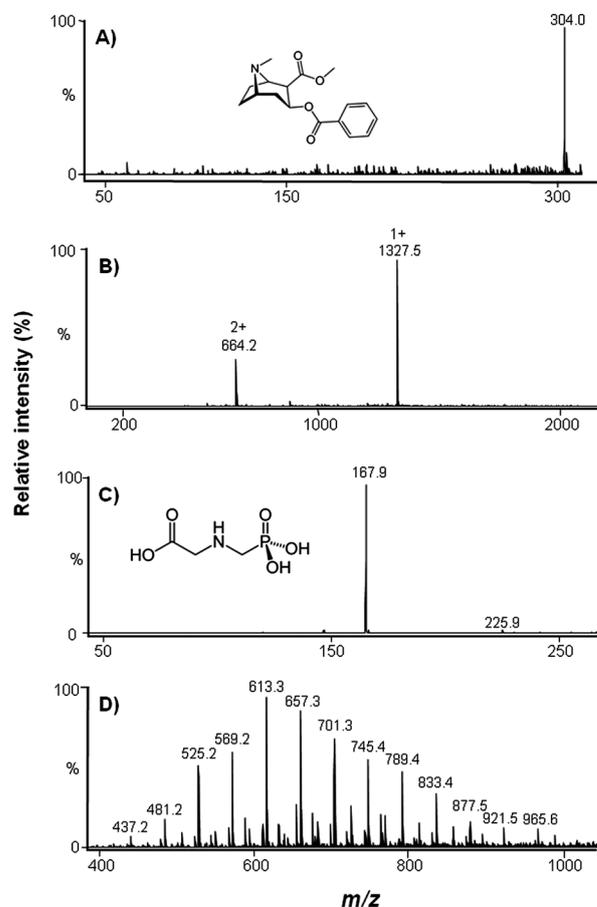


Fig. 2 V_L -EASI mass spectrum of (A) a 25 ng mL^{-1} cocaine solution in acidified methanol; (B) an acidified aqueous solution of the synthetic peptide SIS[pT]RK[pY]SPE (150 $\mu\text{g mL}^{-1}$); (C) a basic methanolic solution of glyphosate (50 $\mu\text{g mL}^{-1}$) and (D) an acidified methanolic solution of PEG 600 (50 $\mu\text{g mL}^{-1}$).

with a predominant $[M - H]^-$ ion of m/z 167.9. Fig. 2D shows the V_L -EASI(+)-MS of an acidified methanolic solution of PEG 600 ($50 \mu\text{g mL}^{-1}$) with the correct average mass on m/z 613 and the characteristic oligomeric distribution of PEG oligomers detected mainly as their $[M + \text{Na}]^+$ adducts.

The signal profile was also monitored by means of total ion current (TIC) as Fig. 3 exemplifies for cocaine solutions (25 and 50 ng mL^{-1} in acidified methanol). Baseline signal (A) is first observed as a result of acidified methanol spraying. In (B), the Venturi capillary is being moved from acidified methanol to the cocaine solutions. In (C), cocaine solutions are being sonic-sprayed with Venturi-self-pumping and TIC remains quite constant for *ca.* 20 s, allowing proper MS acquisition.

The desorption/ionization ability of the Spartan V-EASI source was also tested by analyzing solid samples in the V_S -EASI mode. For that, acidified or basic methanol was self-pumped by the Venturi effect using the air flow of *ca.* $300 \mu\text{L min}^{-1}$ provided by the dust cleaner can. The stream of bipolar charged droplets provided by the V_S -EASI spray, as it bombards the surface, caused proper desorption and ionization of the analyte molecules. Fig. 4A shows the V_S -EASI(-)-MS for a commercial acetylsalicylic acid tablet using methanol spiked with 0.1% NH_4OH as the solvent. Note the intense

$[M - H]^-$ ion of m/z 179 as well as that of m/z 137 that corresponds to the free salicylic acid. Fig. 4B shows the V_S -EASI(+)-MS for a commercial sildenafil tablet using acidified methanol as the spray solvent. Note again the intense $[M + H]^+$ ion of m/z 474.7, and the quite reduced level of chemical noise.

We have systematically observed sensitivity and signal-to-noise (S/N) ratios for V-EASI(\pm) similar to that for EASI(\pm).⁶ When the Spartan V-EASI(\pm) source was compared to the archetype V-EASI(\pm) source, for all analytes tested herein running the same solution and using the same MS and settings, quite similar sensitivity and S/N ratios always within the same order of magnitude were observed for many runs in different days and under different source conditions. This is a quite remarkable result for such a compact, portable "Spartan" source, which is certainly subjected to further improvements. A most welcome feature of EASI and consequently of its sister technique V-EASI has been demonstrated not to be related to absolute intensity but rather to much reduced S/N ratios¹ which greatly benefits detectability in ambient MS analysis.

For desorption/ionization in ambient MS, different levels of simplicity (or lack of it) have been observed for the large and fast growing set of available techniques.¹ Among these techniques, some have certainly offered simple and economical platforms, such as those of paper spray ionization (PSI),¹⁰ low temperature plasma ionization (LTP)¹¹ and, more recently, contactless atmospheric pressure ionization (CAPI),¹² and now V-EASI⁶ simplified herein to what seems to be its upmost limit. For high viscosity fluids, extractive ESI¹³ seems mandatory offering also a simple approach for MS analysis. For large, less soluble molecules such as proteins,¹⁴ or for sampling molecules directly from the surface of solutions,¹⁵ more effort seems to be required and laser desorption, for instance, such as in the electrospray-assisted laser desorption ionization (ELDI-MS) technique, seems also indispensable.

Conclusions

A Spartan dual-mode, fully portable, robust, exceptionally easy to assemble and operate, disposable and inexpensive V-EASI source, able to provide stable, low noise and abundant ion signal has been described. It functions properly for both liquid and solid samples providing efficient desorption/ionization for ambient mass spectrometry. The simultaneous self-pumping and sonic spraying provided by the high velocity stream of air generated by a commercial dust cleaner can eliminate the need of electrical pumping, gas cylinders and regulators, and electrical charging of spray droplets normally employed in spray-based ionization techniques. Analyte ions are produced *via* the bipolar stream of the very minute charged droplets produced *via* the voltage-free sonic spray mechanism; hence, the technique is inherently free from electrical discharges or redox interferences. Parts for assembling the Spartan V-EASI source are simple, inexpensive and commercially and readily available, and the low demands and reduced size seem to make this inexpensive disposable source ideal for miniature mass spectrometers. The major remaining task for easy MS analysis is therefore to achieve true simplification of the mass analyzer. For ionization, however, the Spartan EASI source described herein, we argue, offers one of the easiest and cheapest yet efficient ways to make ions for easy ambient desorption/ionization mass spectrometry analysis of both liquid and solid samples.

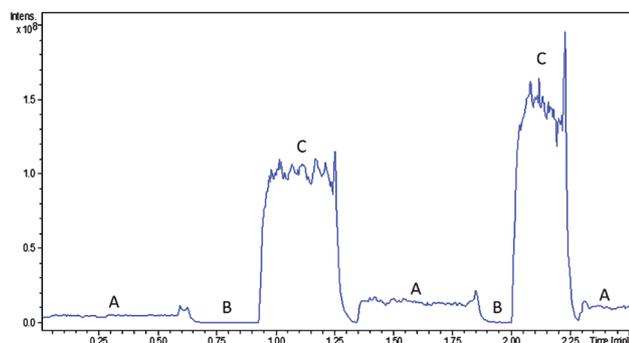


Fig. 3 Signal profile of V-EASI(+)-MS as measured by the TIC for cocaine solutions (25 and 50 ng mL^{-1}) in acidified methanol.

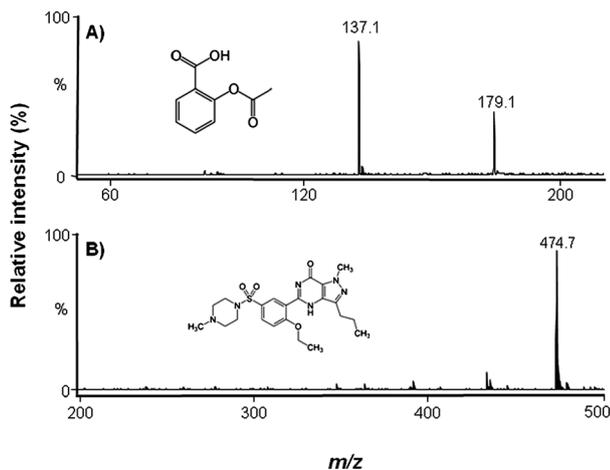


Fig. 4 (A) V_S -EASI(-) mass spectrum acquired from the surface of a commercial acetylsalicylic acid tablet using basic methanol as solvent and (B) V_S -EASI(+) mass spectrum acquired from the surface of a commercial sildenafil tablet using acidic methanol as solvent.

Acknowledgements

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