Direct and fast screening of new psychoactive substances using medical swabs and atmospheric solids analysis probe-triple quadrupole with data-dependent acquisition.

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Results and discussion

Acquisition parameters optimization

The ASAP probe allows the use of a desolvation temperature ramp. Desolvation temperature can be stablished at 70 ºC, and rapidly increased until 600 ºC in 20-30 s. This process allows the analytes with higher volatility to be analyzed by ASAP-MS, as the probe is at low temperature at the beginning of the acquisition. Application of desolvation ramp temperature in ASAP sources can be found in literature, for example, applied to petroleomics for the analysis of different fractions [9]. When a swab is used, the evaporation of the sample does not occur as faster as using the glass capillary, and a fixed desolvation temperature can be used for obtaining closer analyses. **Figure S1** shows the total ion chromatogram (TIC) of a MS scan from *m/z* 50 to 450 of a blank swab with 100 µL of methanol, acquired during 3 min using a 70-450 ºC ramp desolvation temperature (**A**), and a 450 ºC fixed desolvation temperature (**B**). It can be observed that using the ramp temperature, it takes around 60 s to start the evaporation and ionization of the compounds from swab, while using a fixed temperature the evaporation starts at around 30 s. For this reason, a fixed desolvation temperature at 450 ºC, and an acquisition time of 1.5 min were selected for the analysis using swab-ASAP.

When using DDA acquisition mode, it is important to stablish an *m/z* exclusion list to avoid unnecessary MS/MS switches produced by ions coming from the system. Nevertheless, for the analysis of NPS (and using our swabs) it was not considered necessary. **Figure S1C** shows the MS scan spectrum from a blank swab with 100 µL of methanol and 450 ºC desolvation temperature. It can be observed that major ions coming from the system were observed below *m/z* 170. Anyway, if the swab type is changed, the presence of background ions should be assessed. Limiting the survey MS scan from *m/z*

170 to 450 does not affect the detection of known NPS, as their protonated molecules present *m/z* values within this range.

Once stablished the survey MS scan parameters, the MS/MS acquisition parameters were explored. The *m/z* range was stablished from 60 to 450, in order to detect all the product ions produced. A collision energy of 25 eV was selected as a compromise value, in order to obtain enough product ions with a wide *m/z* range for all NPS. The acquisition of MS/MS data also allows the use of on-line spectral MS/MS databases for the tentative identification of the compound, such as METLIN (https://metlin.scripps.edu/) or MassBank (https://massbank.eu/), if the spectrum of the compound of interest is available in these databases.

As the signal produced by the evaporation/ionization of the compounds from the swab was constant during all the analysis time, only one *m/z* value was selected for automatic MS/MS in each survey scan. Additionally, an exclusion time of 10 s for the previously detected precursor ion was stablished, in order to allow the detection of NPS mixtures, even at different concentration. These parameters should not be used for DDA acquisition with chromatographic separation, as the peaks produced are only of few seconds. **Figure S2A** shows the TIC of the automatic CID MS/MS acquisition of an herbal blend sample containing two synthetic cannabinoids. The observed "peaks" are produced when the MS/MS of the protonated cannabinoids are automatically acquired, and it can be also observed the 10 s exclusion time from the last measured *m/z* value. The extracted ion chromatograms (EIC) of specific product ions of these compounds illustrate that the exclusion time used allows the automatic MS/MS acquisition for both compounds, even in mixtures. **Figure S2B** shows the automatic MS/MS spectra acquired for the protonated molecules of JWH-081 and JWH-203, illustrating that the method is suitable for the analysis of mixtures.

Building the spectra library

Once optimized the swab-ASAP-MS/MS DDA parameters, the MS/MS spectra of all NPS available in our laboratory were acquired, in order to create an MS/MS library for a direct compound identification.

Solid samples were directly analyzed by swab-ASAP-MS/MS, following the procedure described in the sample treatment section. Once acquired the DDA data, MS/MS spectra acquired were manually checked, selecting one spectrum for automatic library search. The library was created using the MassLynx Library utilities. For each compound, MS/MS spectrum, name, elemental composition and molecular weight were included in the library. Up to 90 compounds, including synthetic cannabinoids, synthetic cathinones, amphetamines, tryptamines and opioids were included in the spectral library.

Once the library was completed, it was indexed and then converted to the NIST format, required by the MS Search software.

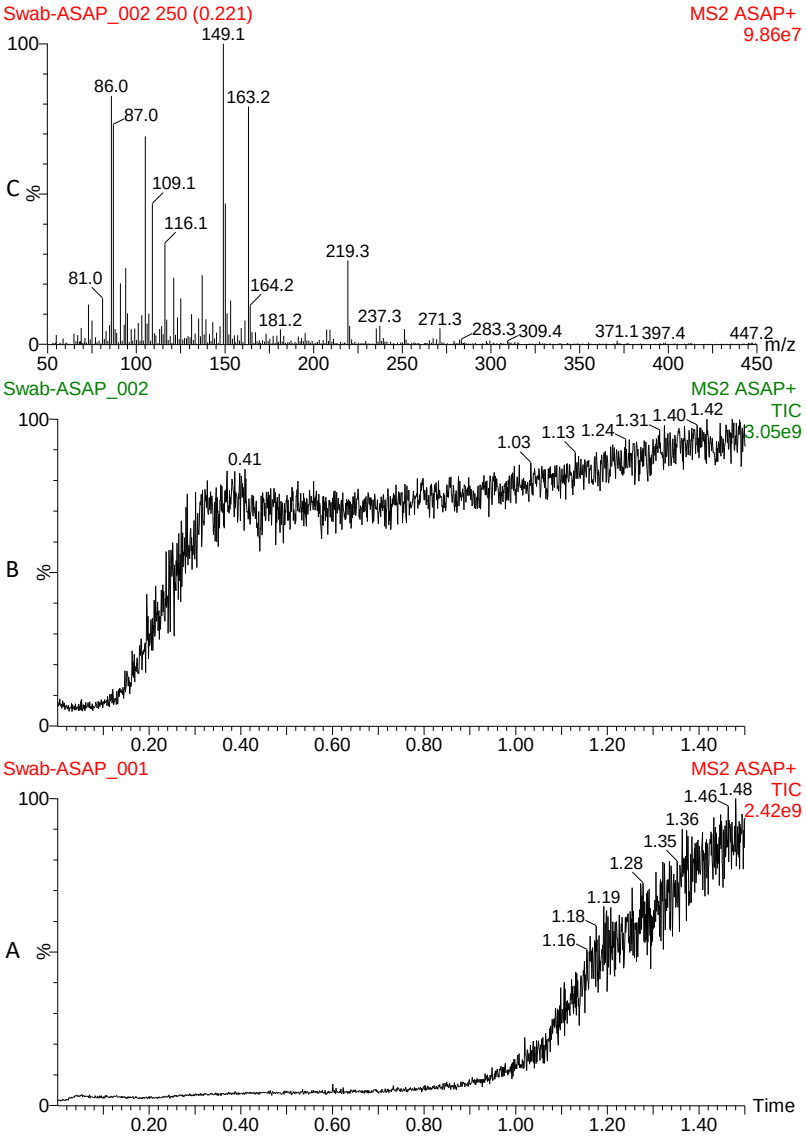

Figure S1. Swab-ASAP source conditions optimization. **A** Scan of a blank swab using a desolvation ramp temperature from 70 to 450 ºC. **B** Scan of a blank swab using a fixed desolvation temperature maintained at 450 ºC. **C** Spectrum of a blank swab.

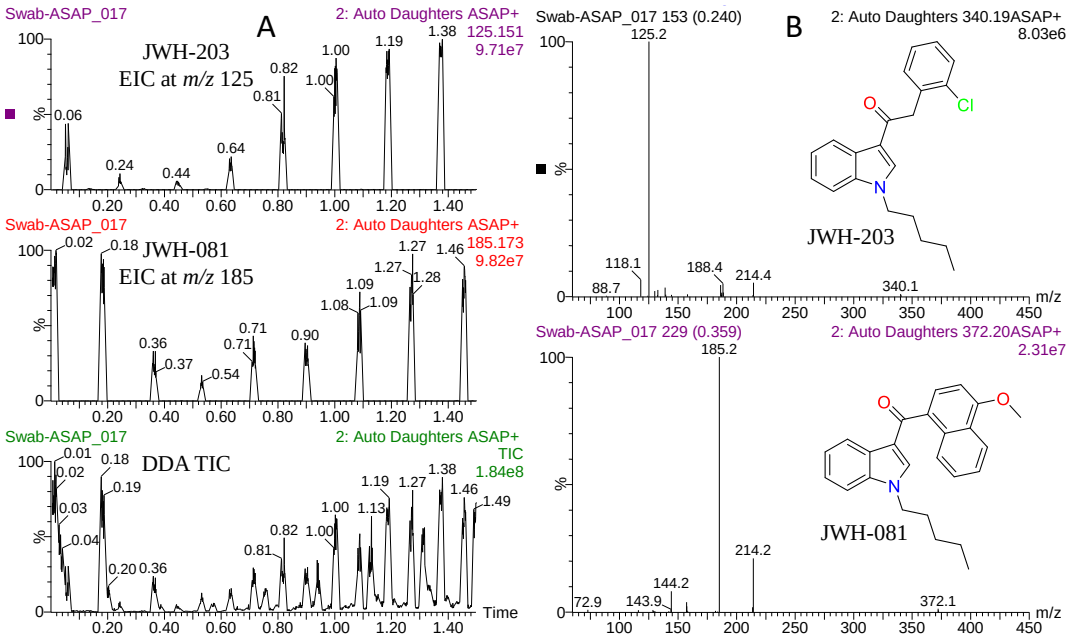

Figure S2. Detection of two synthetic cannabinoids in an herbal blend sample by swab-ASAP-MS/MS DDA. **A** TIC of the DDA function, EIC of product ion *m/z* 185 from JWH-081, and EIC of product ion *m/z* 125 from JWH-203. **B** Automatic MS/MS spectra of JWH-203 and JWH-081 present in the sample.