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IMPROVING QUALITATIVE CONFIRMATION USING XEVO TQ MS WITH SURVEY SCANNING

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INTRODUCTION

On a conventional tandem quadrupole mass spectrometer, the search for unknowns generally requires multiple injections: one injection in full-scan LC/MS mode followed by a second injection for targeted LC/MS/MS experiments. This results in increased time required to obtain the necessary data, in addition to the time the analyst needs to construct the MS/MS methods.

Real-time data-directed switching simplifies this experimental approach. In data-directed mode, a full spectrum LC/MS run is collected, with an LC/MS/MS experiment triggered if the signal in the LC/MS survey meets preset criteria.

Modern Linear Ion Trap (LIT) mass spectrometers allow the collection of MS, MRM, and MS/MS data in the same analytical run, enabling quantitative and qualitative data to be obtained simultaneously. The duty cycle of these instruments when switching between MS and MS/MS modes is typically 2 to 3 seconds. With modern high-resolution, sub-2 µm particle chromatography, such as UPLC,® peak widths of 2 to 3 seconds are now commonplace, thus with these LIT MS systems this results in just 1 to 2 points across the peak giving poorly defined peaks and possibly missed components.

The Waters® Xevo™ TQ MS is capable of scan speeds up to 10,000 amu/sec. Consequently, it is possible to employ a number of scan functions in a single run while still maintaining good peak characterization with no loss in data quality.

Figure 1. Xevo TQ Mass Spectrometer with ACQUITY UPLC.

EXPERIMENTAL

Survey Scans on Xevo TQ MS

Survey Scans on the Xevo TQ MS allow intelligent switching of LC/MS and LC/MS/MS data in one run, thus improving productivity. Conventional MS or ScanWave™ MS scanning experiments can be used to trigger MS/MS experiments in real time as the peaks are eluting from the LC column. A more targeted screen can also be performed using parent ion or neutral loss spectral acquisition, to screen for compounds that have common structural features.

Conventional product ion or enhanced product ion spectra (ScanWave) data can be generated for all the components present in these complex samples. In ScanWave mode, duty cycle improvements result in signal enhancement in scanning acquisition modes, which facilitates the detection of low-level impurities.

An example of a survey scan for the active pharmaceutical ingredient (API) quetiapine, an antipsychotic medication, is shown in Figure 2, where the initial survey function is ScanWave MS switching to ScanWave DS.

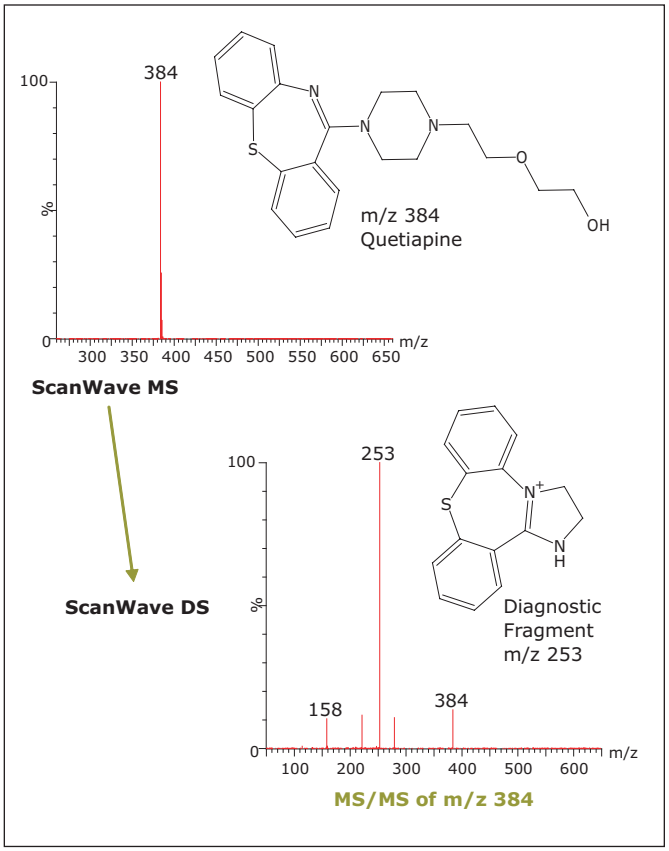

Figure 2. Shown is an example of a Survey Scan of quetiapine (m/z 384) where the initial ScanWave MS Survey function switches to ScanWave DS mode.

In Figure 3, quetiapine ($C_{21}H_{25}N_3O_2S$) was analyzed in survey scan mode. The structure-characteristic fragments of quetiapine[1,2] are m/z 253 ($C_{15}H_{13}N_2S$) and m/z 279 ($C_{17}H_{15}N_2S$). In the above example, a Precursor Ion Scan (m/z 253) was used to trigger the acquisition of a ScanWave product ion scan (ScanWave DS), generating a full product ion spectrum for the compounds potentially related to quetiapine.

More than 20 compounds were observed to have the fragments m/z 253 and m/z 279 as well as another signature fragment m/z 221 ($C_{15}H_{13}N_2$). Shown in Figure 4 are spectra from the chromatographic peaks at retention times 7.86 min, 9.95 min, 10.13 min, 14.01 min, 15.94 min, and 17.52 min, respectively.

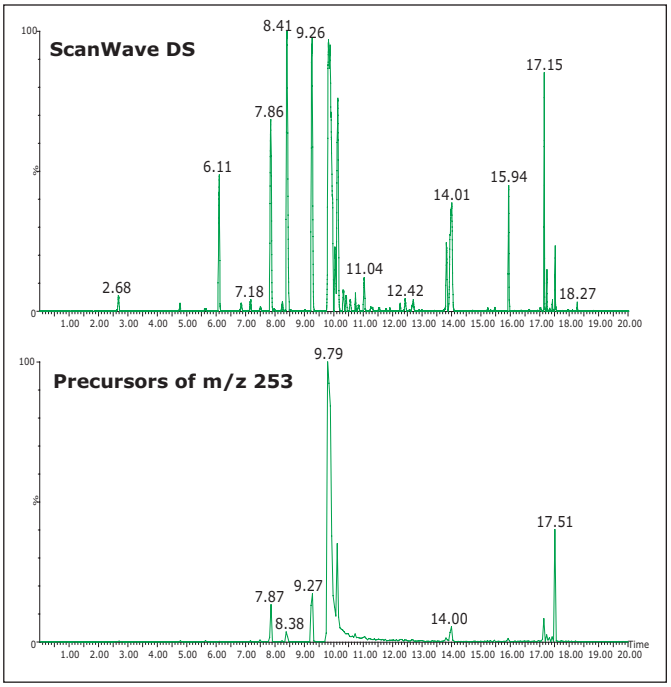

Figure 3. Survey precursor scan of m/z 253 (lower trace) switching to ScanWave DS.

Included are the API, quetiapine, and the previously-characterized[1,2] quetiapine carboxylate and bis (dibenzo) piperazine, as well as three unknown compounds that have similar fragmentation patterns.

This information was obtained from one Survey experiment without the need for extra confirmatory MS/MS analyses. This allows the analyst to acquire important structural information in a single run.

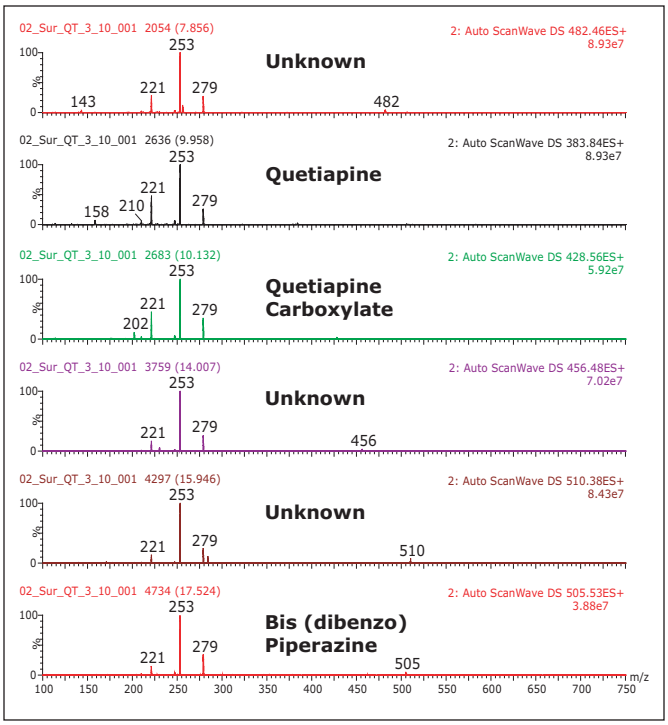

Figure 4. UPLC/MS/MS spectra in ScanWave DS mode from selected chromatographic peaks shown in Figure 3 (top).

CONCLUSION

The Waters Xevo TQ MS, with its unique collision cell design, where the collision gas is always on, facilitates the simultaneous acquisition of MS and MS/MS data in one LC/MS run. Its high scan speed allows for these experiments to be performed with sufficient points across the peak to accurately define the narrow peaks produced by UPLC. This capability facilitates data-directed experiments, where real-time switching between MS and MS/MS allows more information to be acquired from a single injection. This reduces the need for separate experiments and accelerates the process of structural identification and unknown compound determination.

References

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2. Bharathi Ch, Prabahar KJ, Prasad ChS, Srinivasa Rao M, Trinadhachary GN, Handa VK, Dandala R, Naidu A. Identification, isolation, synthesis and characterisation of impurities of quetiapine fumarate. Pharmazie. 2008 Jan; 63(1): 14-9.

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