

High Mass Resolution is Essential for Confident Compound Detection

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Introduction

Analytical laboratories are under ever-increasing pressure to deliver fast results, while maintaining the highest levels of accuracy and confidence. The majority of these laboratories rely on targeted analytical approaches, using both gas chromatography and liquid chromatography coupled to triple quadrupole mass spectrometry (MS) instrumentation. These techniques cover the wide range of chemical classes to be monitored at the required levels of sensitivity and selectivity. However, they are limited to those compounds in the target list and they require careful optimization of acquisition parameters for each compound. High resolution, full scan mass spectrometry using Orbitrap technology provides a solution to:

- the demand for detection and quantification of a growing number of compounds.
- retrospective analysis of samples long after data acquisition.
- identification and elucidation of the chemical composition and structure of unknown compounds.

Until now, high resolution Orbitrap mass spectrometry has been available only with liquid chromatography and has proven to be a highly valuable analytical technique.¹ Orbitrap mass spectrometry technology has now been coupled to gas chromatography (GC) in the Thermo Scientific™ Q Exactive™ GC hybrid quadrupole-Orbitrap mass spectrometer system. This novel configuration of a benchtop hybrid quadrupole-Orbitrap mass spectrometer opens up new possibilities for GC-amenable compounds. The following examples highlight the benefits of high resolution MS coupled to GC.



Q Exactive GC Orbitrap GC-MS/MS system

The Impact of Mass Resolution on Selectivity for Targeted Analysis

High-resolution, accurate-mass (HR/AM) experiments typically provide a full scan analysis of a sample and, for small molecule analyses, the scan range is typically 50–1000 Da. Orbitrap technology provides the required selectivity to resolve the target compound from other compounds or from matrix ions of similar mass. For targeted compound analysis, the accurate mass of the diagnostic ion is extracted with a narrow mass extraction window (typically <5 ppm). This narrow window is possible only when the instrument provides sufficient mass accuracy, for which high mass resolving power is essential. However, when two mass profiles overlap, the measured mass profile is the sum of the two individual profiles. This overlap results in the incorrect assignment of the mass of the target compound. The problem is demonstrated in Figure 1, where a QuEChERS leek extract in acetonitrile was analyzed four times at resolving powers of 15K, 30K, 60K, and 120K (m/z 200).

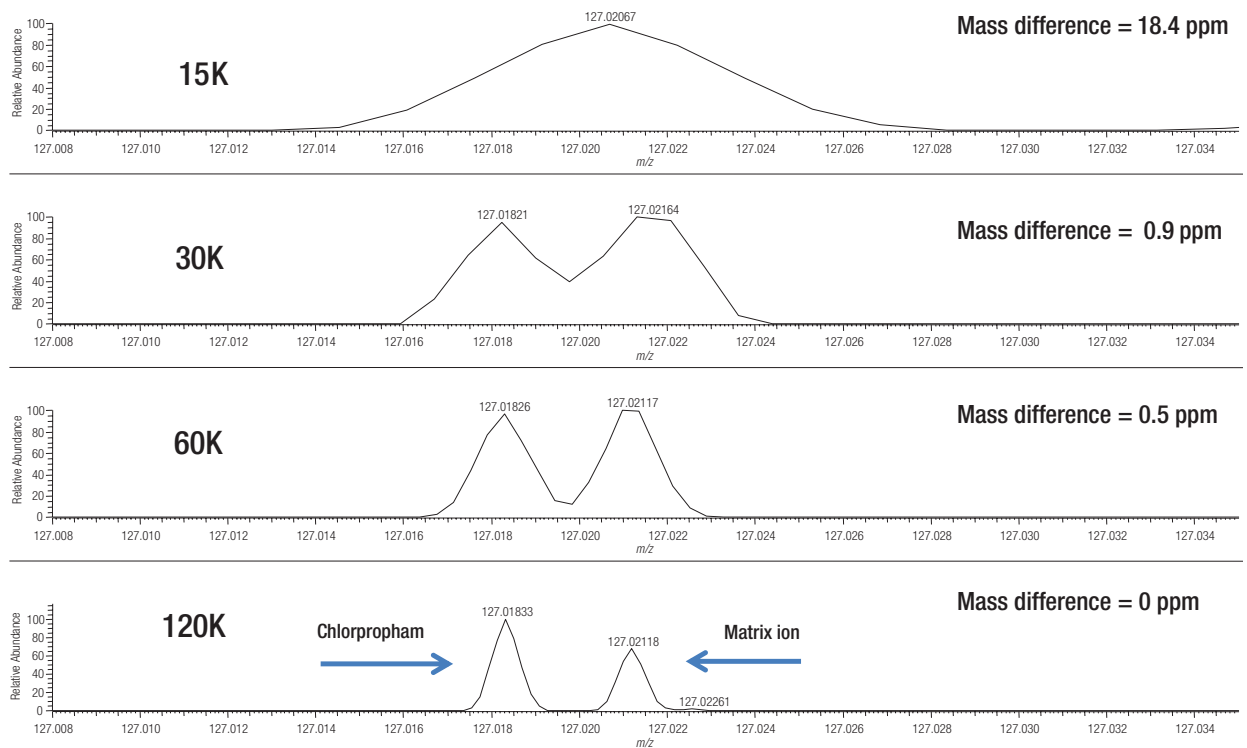


Figure 1. Effect of resolving power on mass accuracy of an analyte in matrix. Mass profiles of chlorpropham 10 ng/g in leek acquired at resolutions of 15K, 30K, 60K, and 120K. Matrix interference at 15K and 30K prevents separation of the pesticide from the interference and higher-than-expected mass difference. Chlorpropham is resolved at 60K and 120K with improvements in mass accuracy. Under normal screening criteria this pesticide would have been missed (false negative).

The mass spectra show the pesticide chlorpropham (m/z 127.01833) and a background matrix ion at a similar mass creating interference. Excellent mass accuracy was achieved for chlorpropham at 60K and 120K, with near baseline resolution. However, at 15K and 30K, chlorpropham was not sufficiently resolved from the interference, resulting in a poorer mass accuracy assignment. At 15K, the mass accuracy was significantly affected with a value of 18.4 ppm mass difference. Under typical screening criteria of <5ppm, and even under a wider tolerance of 10 ppm, this mass difference would have resulted in a false negative (non detection) for this pesticide. This example clearly shows that a minimum resolving power is needed. The required resolving power depends on the complexity of the sample being analyzed and the concentration of both target analytes and interferences.

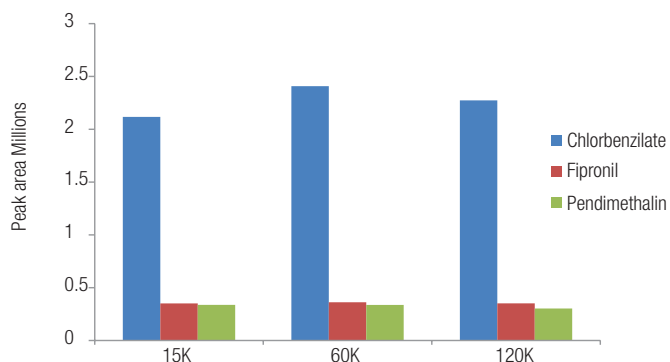


Figure 2. Chlorbenzilate, fipronil, and pendimethalin in a QuEChERS carrot extract at a concentration of 10 ng/g showing peak area responses obtained at 15, 60, and 120K FWHM resolution (m/z 200). Sensitivity is maintained across the resolution modes for both high and low responding analytes. A minimum of 12 scans/peak was maintained.

Maintaining Sensitivity at High Resolution

With other types of GC-MS technology, increasing mass resolution results in a decrease in ion transmission. Consequently, the precision of the measurement can be affected. For low-level targeted compound screening and quantification in complex matrices, it is essential to maintain instrument sensitivity while operating at high resolving power. In Figure 1, the need for high resolution was demonstrated. While resolution is extremely important, it is also essential to maintain sensitivity at the higher resolution modes of 60K and 120K. The Q Exactive GC system does not lose signal intensity as significantly with increasing resolution as other types of mass spectrometers. Figure 2 shows an example of three pesticides (chlorbenzilate, fipronil, and pendimethalin) and the corresponding peak area responses at a concentration of 10 ng/g in carrot QuEChERS acetonitrile extracts. These extracts were analyzed at resolution modes of 15, 60, and 120K in full scan. Absolute peak areas are maintained across the resolution modes. This consistency provides the superior mass resolution required for excellent mass accuracy, without sacrificing sensitivity.

High Resolution for Unknown Compound Identification

One of the advantages of having full scan, accurate mass capabilities is that data can be mined retrospectively and unknown peaks can potentially be identified. The mass accuracy of an ion allows elemental compositions to be proposed based on the measured accurate mass and isotopic pattern. The number of possible chemical formulae proposed is based on the elements used in the calculator and the quality of the spectral data. High resolution measurements that consistently provide sub-1-ppm mass accuracy accelerate the identification process by reducing the number of proposed formulae to a manageable number. This process is illustrated in Figure 3, where an ion at m/z 304.10058 was submitted to the elemental formula calculator and hits were reported using the following elements Carbon 1-50, Hydrogen 1-50, Oxygen 1-20, Nitrogen 1-20, Phosphorus 1-10, and Sulphur 1-10.

Different ppm mass tolerances from 0.5 to 10 ppm were used to suggest possible formulae. The number of hits is reported in Figure 3. As expected, the wider the tolerance, the greater the number of suggestions. At 10 ppm, 60 possible hits are proposed. Even at a relatively low value of 3 ppm, 20 elemental formulae fit the criteria. However, with the sub-ppm mass accuracy expected from the Q Exactive GC system, the number is limited to two formulae at 0.5 ppm. The top suggestion for this mass is $C_{12}H_{21}N_2O_3PS$, with a mass accuracy of 0.3 ppm and, when submitted to the ChemSpider online database, the top hit returned is the pesticide diazinon. This identification can be further confirmed by investigation of the fragment ions, matching with spectral libraries as data are acquired using electron impact (EI).

Conclusion

- With unmatched routine high resolving power and consistent sub-ppm mass accuracy, the Thermo Scientific Q Exactive GC mass spectrometer is a unique laboratory tool suitable for compound discovery, screening, quantitation, compound identification, and structural elucidation applications.
- Routine mass resolution of at least 60,000 FWHM (at m/z 200) was required to resolve chlorpropham from background interfering ions of a similar accurate mass. This resolution is essential for the confident detection of compounds.

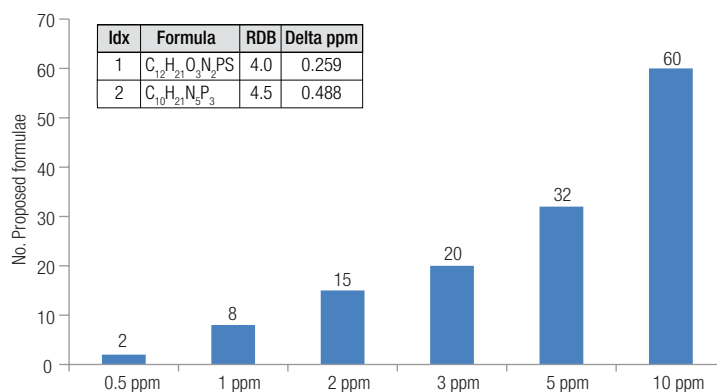


Figure 3. Number of suggested elemental compositions for m/z 304.10058 with different mass tolerances applied. Inset shows the top two hits at 0.5 ppm.

- The Q Exactive GC system provides high sensitivity in complex matrices and importantly, the sensitivity is maintained across all resolution modes used (15–120K FWHM at m/z 200).
- Excellent sub-ppm mass accuracy accelerates the identification of unknown peaks by allowing the use of narrow mass tolerances.

References

1. Thermo Scientific Application Note 617: Quantitative and Qualitative Confirmation of Pesticides in Beet Extract Using a Hybrid Quadrupole-Orbitrap Mass Spectrometer. San Jose, California, USA and Bremen, Germany. [Online] <http://www.thermoscientific.com/content/dam/tfs/ATG/CMD/cmd-documents/sci-res/app/ms/lc-ms/Orbitraps/AN-617-LC-MSMS-Pesticides-Beets-AN64284-EN.pdf> (accessed May 1, 2015).

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