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Orbitrap HRMS for compound-specific isotope measurements: applications to pharmaceuticals and curcumin

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Summary: *Orbitrap HRMS was evaluated for compound-specific isotope analysis of chloroquine in falsified medicines and curcumin in curcuminoid samples. Carbon and chlorine isotope information was obtained from selected ions and fragments, supporting authentication and sample comparison with limited sample preparation.*

Keywords: *Orbitrap HRMS; stable isotope analysis; authentication*

Introduction
Conventional bulk isotope analysis provides an overall value for the sample and may be influenced by the presence of multiple ingredients. Compound-specific measurements overcome this limitation but often require laborious isolation or purification. Orbitrap high-resolution mass spectrometry offers a complementary approach based on the accurate measurement of monoisotopic ions and their heavy-isotope isotopologues.

Experimental
Two applications were investigated. Falsified antimalarial tablets were first screened by LC–Orbitrap-MS to identify and semi-quantify active pharmaceutical ingredients. Chloroquine-containing samples were then analysed by infusion-Orbitrap-MS, targeting the molecular ion and its ^{13}C- and ^{37}Cl-containing isotopologues. Curcuminoid samples of natural, synthetic and unknown origin were analysed by measuring the ^{13}C isotopic abundance of intact curcumin and four major product ions generated by MS^2 fragmentation. In both studies, the areas of the monoisotopic and heavy-isotope ions were extracted, and their ratios were converted into delta values.

Results and discussion
For chloroquine, the combined $\delta^{13}C$ and $\delta^{37}Cl$ values revealed at least three groups of samples, suggesting possible differences in production batches, raw materials or manufacturers. For curcumin, $\delta^{13}C$ values differed significantly between natural and synthetic samples. MS^2 experiments also provided isotope information from different portions of the curcumin structure, improving discrimination between origins.

Conclusions
Orbitrap HRMS enables compound-specific isotope information to be obtained from selected target molecules with limited sample preparation. The technique combines molecular selectivity, multi-element isotope measurement and fragment-level information, providing a promising complementary tool for authentication, forensic comparison and source investigation.