

LC-MS/MS ANALYSIS OF PHARMACEUTICAL COMPOUNDS ON A HYBRID QUADRUPOLE ORTHOGONAL ACCELERATION TIME-OF-FLIGHT MASS SPECTROMETER (Q-Tof)

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Recent trends in the pharmaceutical industry have driven mass spectrometry to provide more information on drug candidates from increasingly smaller amounts of material. Whereas only a few years ago a nominal molecular weight measurement on a minor peak in a UV chromatogram was considered satisfactory, this is no longer the case and as much information as possible is required by regulatory bodies.

Triple quadrupole mass spectrometers coupled to liquid chromatographs are used widely for studying complex mixtures by LC-MS/MS. Whilst being able to provide low resolution nominal mass data on the components present and confirm their structural identities by low energy MS/MS studies, they do not provide sufficient mass accuracy to derive useful empirical formulae for the parent ions or their fragments. This information can be important in the assignment of impurity structures, or in locating the position of modification for a drug metabolite.

The recent development of a hybrid quadrupole orthogonal acceleration time-of-flight mass spectrometer (Q-Tof) has resulted in increased sensitivity over triple quadrupole mass spectrometers, improved resolution (>5000 FWHM) and due to the simple calibration law allows exact mass measurements, to within 5ppm of the expected values, to be routinely performed.

In this paper high quality MS and MS/MS data were obtained from the on-line LC analysis of an experimental intermediate of a novel drug compound. Data dependent (on the fly) decisions were used to identify and select precursor ions for MS/MS. Exact mass measurements were performed in both MS and MS/MS modes. Data from a series of isomeric impurities where exact mass measurements on the fragment ions in the MS/MS spectra has been used to derive elemental compositions and distinguish unique structural characteristics, will be presented.