DRUG DEVELOPMENT SOLUTIONS
Part of Alliance Pharma, Inc.

Structural Elucidation

Characterisation and monitoring of impurities using Ultra-Performance Liquid Chromatography and High Resolution Mass Spectrometry (UPLC-HRMS).

Knowledge of the impurities and degradation profile of drug substance and excipients is critical in understanding the stability, safety and efficacy of a bio/ pharmaceutical drug product.

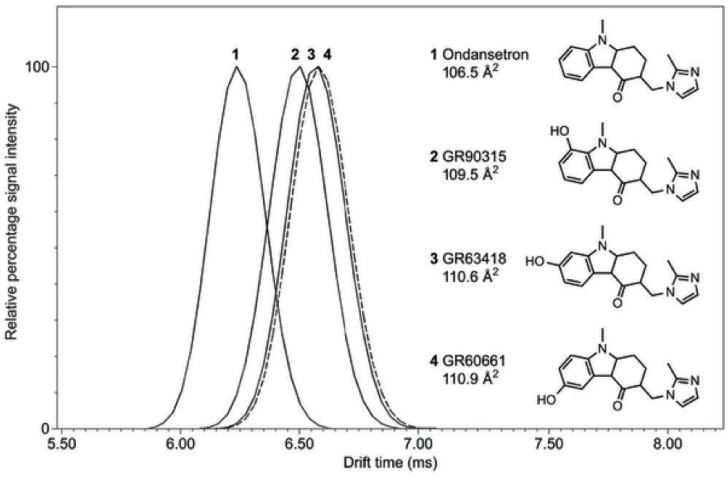

Figure 1: Structural elucidation of isomers using the ion mobility technology

CENTRE OF EXCELLENCE
IMPURITY AND CONTAMINATION

Our Impurity and Contamination Centre of Excellence are experts in the identification and quantification of trace impurities in a wide range of materials used throughout the global pharmaceutical and healthcare sectors.

Identification of impurities and degradation products requires multiple analytical techniques to establish a significant degree of certainty. Structural elucidation of unknown substances such as synthetic impurities is an important factor to refining pharmaceutical drug efficacy and safety attributes.[1] The key in resolving these challenging structural identifications has been development of innovative and powerful instrumentation. Skilled scientists can then use experience and software to interrogate and interpret the data generated.

The result is the ability to conclude with relative certainty the nature of the products theorised. The combination of mass spectrometry, specifically high resolution (Quadrupole-Time-of- Flight) with Ion mobility (Figure 1) and nuclear magnetic resonance (NMR), allows for this complete structural understanding.

Our cutting-edge laboratories are well equipped with the latest technology to support your structural elucidation studies.

The combination of these instruments makes it possible to confirm with a high degree of certainty and accuracy the full structural form of any previously unidentified component.

Reference:
1. Ahuja, S. and Alsante, K. (2003) Handbook of Isolation and Characterisation of Impurities in Pharmaceutical Compounds; Elsiver.

Case example

Challenges

One example of quantifying impurities at very low levels involved an unknown degradation product of a human peptide hormone. The sponsor had observed a new peak in the standard LC-UV chromatography during the stability assessment of the product.

Science

The sponsor's method was established on an Acquity UPLC coupled to a Waters SynaptTM G2 mass spectrometer. The method was modified for maximum sensitivity and the data interpretation focussed on specific regions within the chromatographic run. Assessment of 3D data provided information to identify ions of interest. These ions were selected for MS/MS fragmentation which provided high resolution, accurate mass data (Figures 2 and 3).

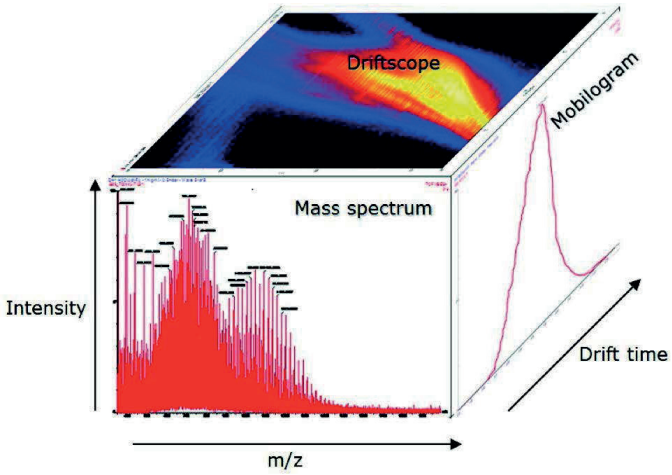

Figure 2: Data showing driftscope intensity, retention time, peak shape and mass spectrum

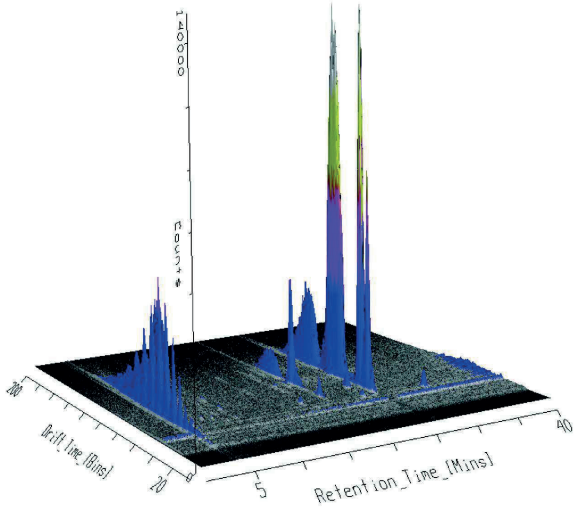

Figure 3: A 3D data file of the degradation of a human peptide hormone in solution

Solution

The data identified peptide sequences related to the human peptide hormone. These peptide sequences identified a degradation pathway for this compound and highlighted a potential stability issue that previously had not been considered.

A value added service

Following identification of unknown species we possess the capability to develop and validate organic assay and related impurity methods to support release testing and stability studies. Our structural elucidation capabilities have also complemented and strengthened our Extractables and Leachables services in identifying unknown compounds from extraction studies.

Let's discuss your project:
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