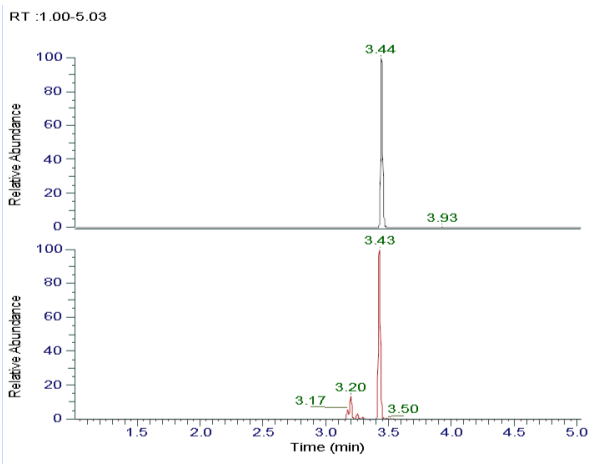
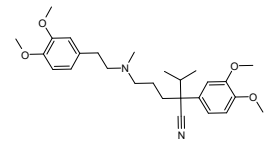
Metabolite Identification

Understanding the metabolic fate of a potential drug candidate is an important part of the drug discovery and development process but the reasons for investigating this vary throughout the life of a drug discovery campaign. In early discovery, the objective is to design potent, metabolically stable compounds and knowing the major route of metabolism quickly can help the chemists achieve this as part of the design, make, test cycle.

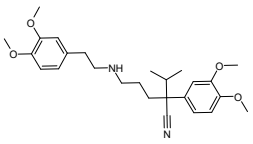
The intrinsic clearance assay is used to determine metabolic stability. For compounds of interest, a later time point sample can be reanalysed on an extended analysis method using a Thermo Scientific™ Exploris 120 Orbitrap to allow rapid identification of the major route(s) of metabolism.



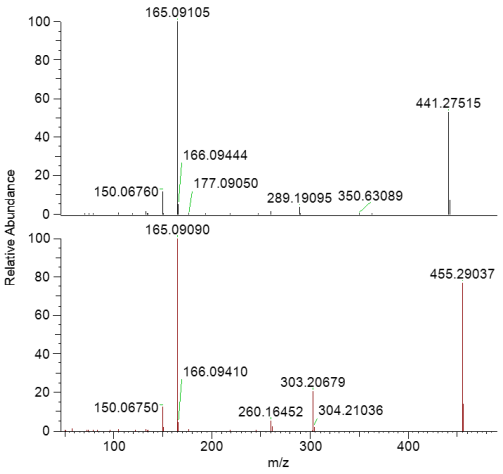
Extracted ion chromatograms for marker compound (top) and its main metabolite (bottom) from the 20 minute sample from the intrinsic clearance assay in rat microsomes at 1 µM



Marker Compound



M1: N-demethylated



Product ion spectra for marker compound and its major metabolite from the 20 minute sample from the intrinsic clearance assay at 1 µM

As projects progress, the focus shifts to identifying the metabolic profile in human. Initially in hepatocytes, the metabolic profile is compared to other species that may be used for safety studies. This enables the confirmation of metabolite coverage and identifies any human specific metabolites in addition to flagging any possible reactive species such as acyl glucuronides or glutathione related metabolites.

Depending on need, different levels of detail for the analysis and reporting can be provided:

Tier 1-2	Early discovery highlights metabolic liabilities to the team enabling stability improvements.
Tier 3	Mid-stage discovery to quickly obtain a more detailed picture of the metabolic profile.
Tier 4	Late-stage discovery to compare the human metabolic profile in hepatocytes with other species to assist in identifying appropriate species for safety studies.
Tier 5	Late-stage discovery or development to determine metabolic profile from in vivo studies.

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All our assays can be customized to answer specific project questions

Contact us for more information on standard or customized assay formats