cyprotex AN EVOTEC COMPANY

*In vitro* **ADME**

# Metabolite Profiling and Identification using High Resolution Accurate Mass Spectrometry

## Background Information

'We encourage the identification of differences in drug metabolism between animals used in nonclinical safety assessments and humans as early as possible during the drug development process. The discovery of disproportionate drug metabolites late in drug development can potentially cause development and marketing delays.'

[1]FDA Guidance for Industry: Safety Testing of Drug Metabolites (February 2008)

- Understanding which metabolites are likely to be formed *in vivo* is essential for interpreting pharmacology, pharmacokinetic and toxicology data.
- Cyprotex's metabolite profiling and identification service uses either the AB Sciex TripleTOF® 6600 or the Waters Xevo® G2-S QTof to determine high resolution accurate mass of any metabolites – leading to increased sensitivity and enhanced structural characterisation.
- Service can be combined with the LabLogic Beta-Ram® for radiochemical detection and quantification of metabolites or with gas chromatography (APGC) for analysis of different types of chemistry.
- Critical information on the formation of metabolites including, where appropriate, both Phase I and Phase II metabolism, and comparison of drug metabolism routes in different species is provided.
- Metabolites can be investigated in a number of different matrices including *in vitro* microsomal incubations, hepatocyte incubations, expressed enzyme incubations as well as *in vivo* samples.
- Cyprotex offers a range of metabolite profiling services depending upon the level of detail and interpretation required.

## Protocol

**Matrices Analysed**
Typically, microsomal incubations, hepatocyte incubations, expressed enzyme incubations, and plasma (others available on request)

**Instruments**
AB Sciex TripleTOF® 6600
Waters Xevo® G2-S QTof
LabLogic Beta-Ram® (for radiolabelled studies)

**Data Delivery**
Various options are available depending on the depth and breadth of metabolite profiling or identification that is required. Typically data is delivered as either:

- Summary document with chromatograms and ion spectra
- Customised report without structural elucidation
- Comprehensive report with structural elucidation

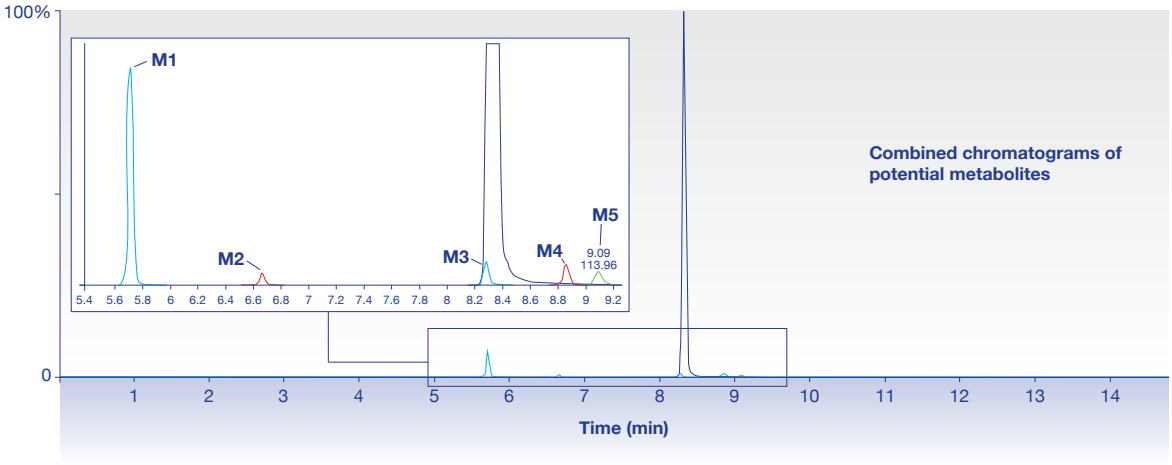
Data delivery format is discussed with the client prior to study initiation. This way the appropriate information is returned in the most timely and cost effective manner

To find out more contact **enquiries@cyprotex.com**

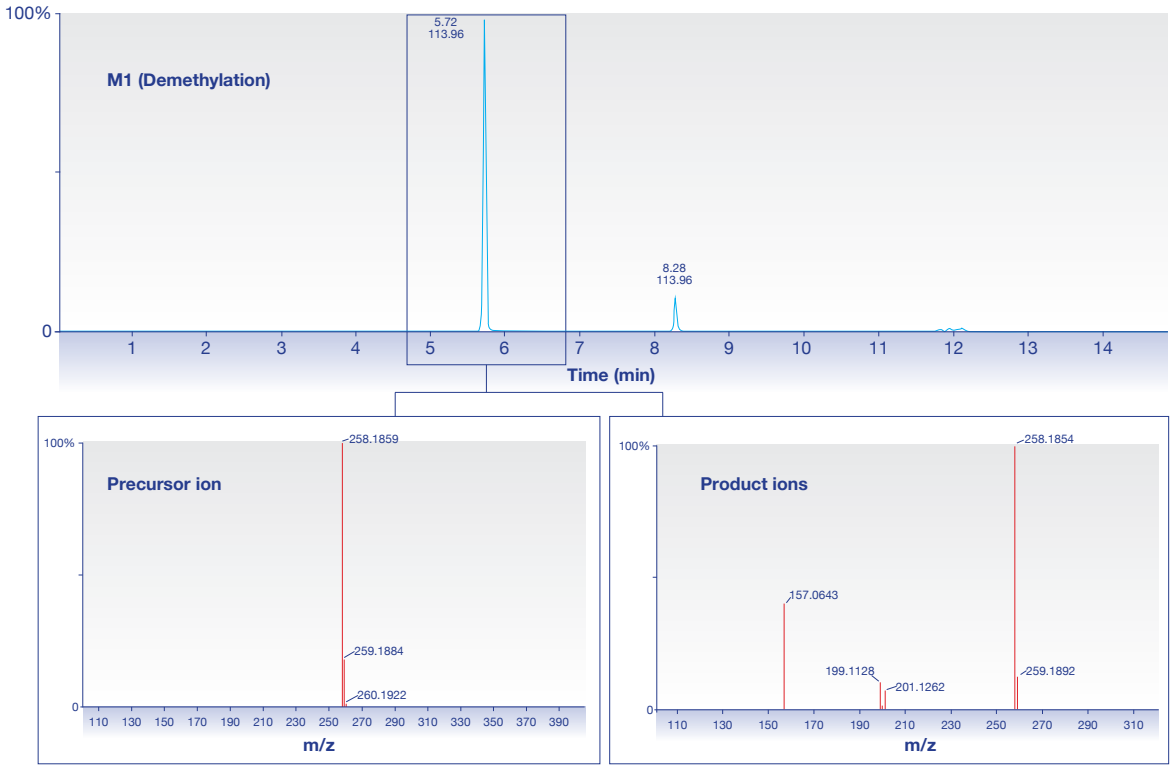
**Figure 1**

Metabolite profiling of dextromethorphan metabolism in human liver microsomes.

A summary of all potential metabolites is provided.




| Name | Formula | Mass Difference | m/z found | Mass error (ppm) | Identifier | Rt (min) |
|---|---|---|---|---|---|---|
| Parent | $C_{18}H_{25}NO$ | - | 272.02010 | -1.5 | - | 8.33 |
| Dehydration | $-H_20$ | -18.0118 | 254.1896 | -4.9 | M5 | 9.09 |
| Demethylation | $-CH_2$ | -14.0159 | 258.1855 | -1.0 | M3 | 8.28 |
| Demethylation | $-CH_2$ | -14.0154 | 258.1860 | 0.9 | M1 | 5.72 |
| Oxidation | +O | +15.9935 | 288.1949 | -1.4 | M4 | 8.85 |
| Oxidation | +O | +15.9946 | 288.1960 | -0.3 | M2 | 6.67 |




References

[1] FDA Guidance for Industry: Safety Testing of Drug Metabolites (February 2008)