



Metabolic Profiling and Metabolite Identification Studies

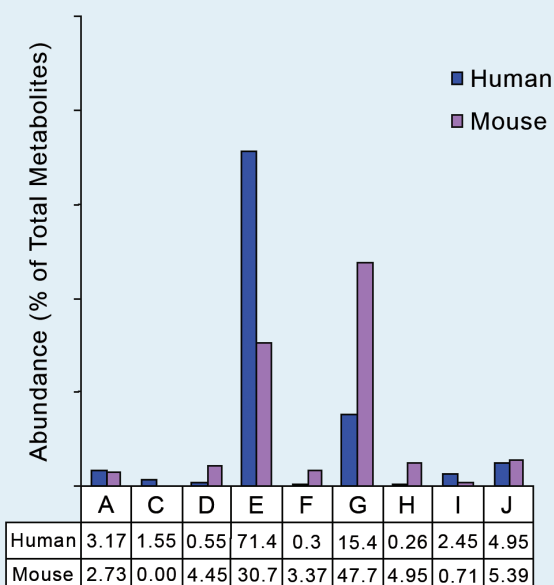
The role of metabolites in drug-induced toxicity is a major concern to the pharmaceutical industry¹⁻³. Knowledge of the types of metabolites formed and species differences in metabolite formation is critical in assessing metabolite-related toxicity. *In vitro* methods using microsomes or hepatocytes can provide valuable information early in the drug development process.

Celsius Development Services provides metabolic profiling and metabolite identification services to help you determine the metabolic fate of your test compound. Results from these studies may be used to select preclinical toxicology species.

Increasing discovery. Advancing development.

Metabolic Profiling and Metabolite Identification Studies

Sample Metabolic Stability Data



Species Comparison of Test Compound Metabolites Following Incubations with Hepatocyte Suspensions from Human vs. Mouse

Experimental Features

- Test system: animal or human liver microsomes or hepatocytes
- Incubation of test system with test compound at two concentrations
- Metabolic profiling analysis by LC/MS
- Identification of up to five major metabolites using MS/MS analysis
- Microsomes or hepatocytes from various animals may be used to evaluate species differences

Protocol

This study is performed in two phases: 1) metabolic profiling; followed by 2) metabolite identification. Liver microsomes or hepatocytes are incubated with the test compound at two concentrations. Samples are analyzed by reverse phase HPLC. Exact conditions are selected based on the chemistry of the test compound and in consultation with the Sponsor. A UV profile of the samples is obtained followed by MS analysis using a Micromass® Q-ToF-2 mass spectrometer capable of conducting accurate mass measurement. Further structural characterization of up to five metabolites by MS/MS analysis is conducted following evaluation of the data from the metabolic profiling experiment.

We customize the protocol to meet your specific needs.

References

- 1 Sharer, J.E.; Shipley, L.A.; Vandenbranden, M.R.; Binkley, S.N.; Wrighton, S.A. Comparisons of phase I and phase II in vitro hepatic enzyme activities of human, dog, rhesus monkey, and cynomolgus monkey. *Drug Metab. Disp.* **1995**, 23, 1231–1241.
- 2 Lin, J.H. Species similarities and differences in pharmacokinetics. *Drug Metab. Disp.* **1995**, 23, 1008–1021.
- 3 Smith, D.A.; Obach, R.S. Seeing through the mist: Abundance versus percentage. Commentary on Metabolites in Safety Testing. *Drug Metab. Disp.* **2005**, 33, 1409–1417.

 | Development Services

1450 South Rolling Road, Baltimore, MD 21227, USA T +1 410 455 1242 F +1 410 455 1245 E customerservice@invitroretech.com