



Metabolic Stability Studies

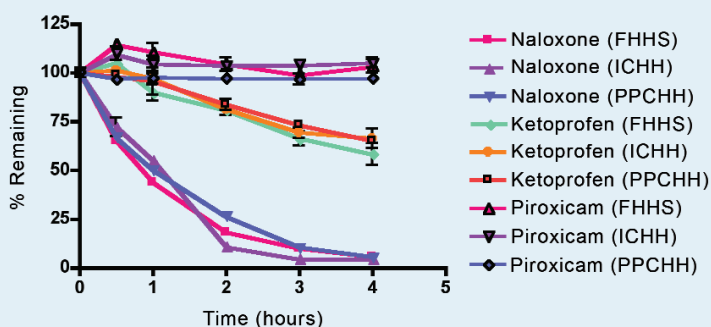
The metabolic stability of a drug candidate impacts its bioavailability and half-life *in vivo* and should be evaluated early in the drug discovery and development process¹. *In vitro* methods using liver microsomes or hepatocytes provide valuable insights into metabolic stability and aid in the selection of drug candidates with favorable pharmacokinetic properties.

Celsis Development Services provides metabolic stability testing services to determine parameters such as rate of metabolism, half-life ($t_{1/2}$), and intrinsic clearance (CL_{int}).

Increasing discovery. Advancing development.

Metabolic Stability Studies

Sample Metabolic Stability Data



Metabolic Stability of Model Pharmaceuticals in Human Hepatocytes. Piroxicam, ketoprofen, and naloxone represent compounds with low, moderate, and high clearance, respectively.

Abbreviations: fresh human hepatocyte suspensions, FHHS; individual cryopreserved human hepatocytes, ICHH; pre-pooled cryopreserved human hepatocytes (LiverPool™), PPCHH.

Experimental Features

- Test system: animal or human liver microsomes or hepatocytes
- Incubation of test system with test or control compound at one concentration for multiple time points
- Metabolic stability of test compound is compared with control compounds with low, moderate, and high clearance
- Microsomes or hepatocytes from various animals may be used to evaluate species differences in metabolism
- Alternate test systems (e.g., S9 fractions, recombinant CYP enzymes, extrahepatic subcellular fractions) may be used per your request

Protocol

Liver microsomes or hepatocytes are incubated with the test compound for a series of time points. Control compounds with known low, moderate, and high clearance are included for comparison with the test compound. Microsomes, which are subcellular fractions, contain phase I oxidative enzymes only and require cofactors to function. Thus microsomes are typically used in first-pass screening for metabolic stability. As intact whole cells, hepatocytes contain the full complement of phase I and II drug-metabolizing enzymes, and are generally used to provide more complete information regarding metabolism of the test compound. Analysis is conducted by evaluating the disappearance of parent compound over time. Microsomes or hepatocytes from various animal species may be used to conduct a species comparison with human data.

We customize the protocol to meet your specific needs.

Reference

- 1 Baranczewski, P.; Stanczak, A.; Sundberg, K.; Svensson, R.; Wallin, A.; Jansson, J.; Garberg, P.; Postlind, H. Introduction to in vitro estimation of metabolic stability and drug interactions of new chemical entities in drug discovery and development. *Pharmacol. Rep.* **2006**, *58*, 453–472.