Evaluation of Liver Metabolic Stability

Need

The development of a new drug candidate requires an understanding of its metabolic stability in the liver. Data obtained from these studies can be used to:

- Inform drug design
- Predict intrinsic clearance (Cl_{int})
- Determine half-life ($T_{1/2}$)
- Support preclinical animal testing and IND submissions.

Solution

Our TruVivo® 2D+ hepatic system can add important information to understanding the metabolic stability of a compound as it possesses key liver properties, including phase II metabolism systems and cell uptake and efflux (transporter) pathways, to test extended exposure times in a more *in vivo*-like liver model.

With our *In Vitro* Assay Services team, IND enabling studies testing Cl_{int} and $T_{1/2}$ can be performed with rat and human primary hepatocytes in the TruVivo system, providing a complete and translatable data set for new drug candidates.

Accurate & reliable data

Fast turnaround times

Unsurpassed expertise

Collaborative approach

Basic Study Design

ASSAY PARAMETERS	PROTOCOL
Test system and options	Single or pooled microsomes or primary hepatocytes in suspension, S9, or primary hepatocytes plated
Species	Rat, Dog, Monkey, Human (Human and Rat for TruVivo)
Test Article concentration	1 µM and 10 µM (can vary on request)
Microsomal protein	0.5 mg/mL (can vary on request)
Time points	0, 5, 10, 15, 20, 30, 60 minutes (longer time points, up to 72 hours, available in TruVivo)
Cofactor +/-	1 mM NADPH +/- incubations (microsomes only)
Solvent	DMSO at final concentration 0.2%
Stock solution test article	10 mM in DMSO
Positive and Negative Controls	0 (blank), Positive 2 drugs known activity (e.g. Midazolam and Diclofenac)
Analytical method	LC/MS/MS
Data	Loss of parent (%) vs time, $T_{1/2}$, estimated Cl_{int} (where possible)
Time to Complete	3-4 weeks from initiation
Report	Full written report

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Talk with one of our experts for help with general inquiries, protocol details, or becoming a new client.

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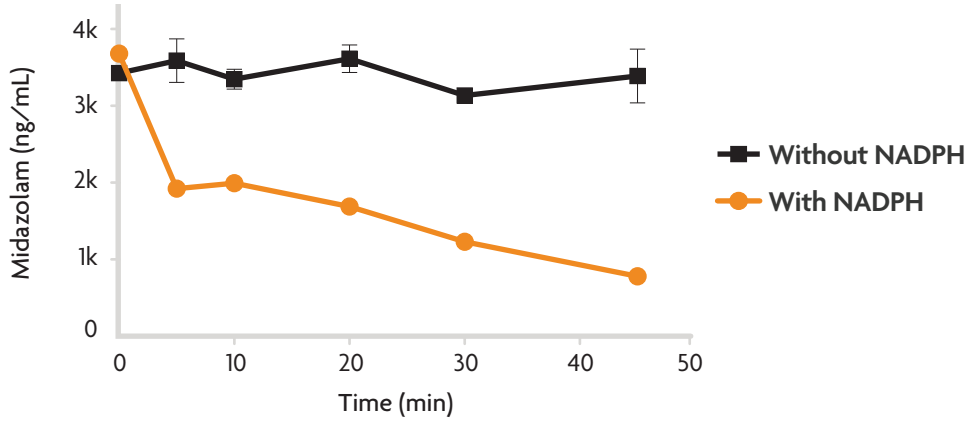
Example Data | Metabolic Stability – Midazolam – Human Microsomes



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