Scaling up the production of human and other mammalian metabolites

Scalable S9 and microsome incubations

Hypha’s scale-up services now include provision of metabolites using a panel of hepatic S9 and microsomal fractions, to complement our successful microbial biotransformation platform. This addition boosts the success rate from 86% to over 90% coverage of target metabolites.

Hypha’s S9 fraction based reactions are scalable to provide multi mg quantities of target metabolites at high purity. The microbial route provides a cost advantage for larger mg to gram scale amounts, as the microbes make their own co-factors.

Our panels can be tailored to generate scaled up amounts of oxidative, glucuronidated, sulfated or thiol-conjugated metabolites. Both approaches offer the advantage of generating Phase I and subsequent conjugated metabolites arising from sequential or multi-step reactions due to intact molecular diversity of the native enzymatic systems.

As part of the new broadened service, we ensure a broad mammalian metabolic coverage comprising 8-10 different species in the initial screen. These are typically evaluated alongside our microbial panels allowing the best yielding and most cost effective process to be scaled up to deliver high purity metabolites. We are successful 96% of the time in scaling up the reaction observed in the initial screen and all purified material is provided back to our clients, even if the yield exceeds that required.

Through availability of all these options, we are able to offer a comprehensive service for obtaining metabolites at whatever scale and route is required.

“We contacted Hypha Discovery to generate specific phase I and phase II metabolite standards in sufficient quantities and purity to allow structural confirmation and quantitation. Hypha exceeded expectations, providing 60mg of a phase I metabolite and over 100mg of a phase II metabolite at high purity. Hypha’s team was a pleasure to work with and communicative and responsive throughout the process. We will undoubtedly be working with Hypha Discovery in the future.”

Jason Boer, Senior Principal Investigator
Incyte Corporation, USA

For more information about our services, contact us at mail@hyphadiscovery.co.uk

We work with 7 out of 10 of the top pharma companies and 4 out of 6 of the top agrochemical companies worldwide. Some of our clients include:

DUPONT  GILEAD  Landou  Bayer  Novartis  Salix  GlaxoSmithKline
Phenex  Incyte  Syngenta  UCB  Syneos  Ferrero

We produce mammalian Phase I and II metabolites using microbial chemistry, mammalian tissue and enzymology expertise:

- For DMPK / ADME / TOX
- For Met ID
- As standards for quantitation
- For bioactivity testing
- For stability studies

Proven Reactions
Methyl hydroxylation
Methylene hydroxylation
Methine hydroxylation
Aromatic hydroxylation
N-oxidation
N-demethylation
O-demethylation
Carbonyl reduction
Heterocycle oxidation (AO)
Aromatic O-glucuronidation
Aromatic N-glucuronidation
Non-aromatic O-glucuronidation
Non-aromatic N-glucuronidation
Acyl-glucuronidation
N-sulfation
O-sulfation
Glycosidation
Thiol conjugation (GSH/NAC)
Sequential reactions e.g. hydroxylation & glucuronidation

8-10 multi-species liver S9 panel
Recombinant CYPS
Tailored microbial panel screen
Scale-up metabolite supply
Lower cost option for multi-lg to g scale

About Hypha Discovery

Hypha Discovery Ltd is a UK-based microbial biotechnology company providing solutions to pharmaceutical and agrochemical R&D partners worldwide through the production of mammalian and microbial metabolites, as well as specialising in microbiably-derived chemicals.