

Phase 1 drug metabolites

Production of human and novel non-mammalian metabolites of cyclosporin A

We produce and scale-up mammalian phase I and 2 metabolites using chemical synthesis, microbial catalysts, mammalian tissue fractions and recombinant enzymes:

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

Proven Reactions

- Methyl hydroxylation
- Methylene hydroxylation
- Methine hydroxylation
- Aromatic hydroxylation
- N-oxidation
- N-methylation
- N-dealkylation
- N-acetylation
- O-dealkylation
- Carbonyl reduction
- Heterocycle oxidation via aldehyde oxidase
- Aromatic O-glucuronidation
- Aromatic N-glucuronidation
- Non-aromatic O-glucuronidation
- Non-aromatic N-glucuronidation
- Acyl-glucuronidation
- Other glycosidations (AgChem)
- N-sulfation
- O-sulfation
- Thiol conjugation (GSH/NAC)
- Transamination
- Amino acid conjugations
- Sequential reactions e.g. hydroxylation & glucuronidation

For more information contact us at mail@hyphadiscovery.com

ABOUT HYPHA DISCOVERY

We are a UK-based CRO providing solutions to pharmaceutical and agrochemical clients globally through the production, purification and characterization of metabolites of drugs and agrochemicals. We have delivered projects for 8 of the top 10 pharma companies and 5 out of 6 of the top agrochemical companies in provision of metabolites.

It is well known that metabolites of drug compounds may have different efficacy and side effects to that of the parent compound. Investigation and production of these metabolites is critical for exploration and understanding of SAR, and to ensure thorough patent coverage. Metabolites can also be sourced to create antibodies used in development of assays for therapeutic drug monitoring.

Production of mammalian metabolites of Cyclosporin A by strains in Hypha's microbial panel

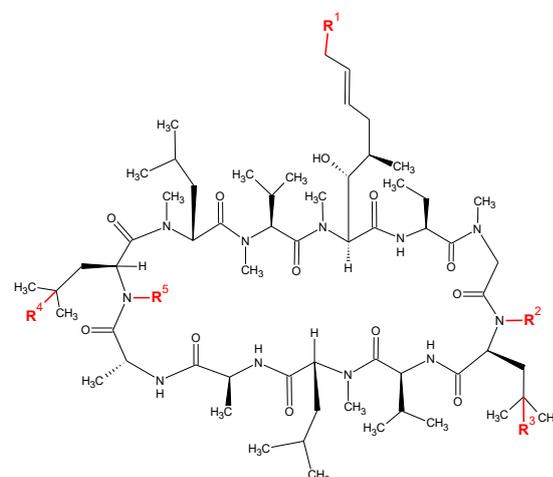
Hypha's has the ability to create both mammalian and microbial metabolites of drug candidates at scale, in order to permit characterization and assessment towards full SAR and patent coverage.

All of the main human metabolites of Cyclosporin A were observed through biocatalysis using Hypha's microbial panel, which results in selective hydroxylation as illustrated below. Additionally we are able to form novel microbial-derived metabolites.

"Hypha Discovery has been a valuable metabolite ID partner. Hypha have provided biotransformation, metabolite purification and structure elucidation answers to some of our most challenging metabolism and metabolite ID problems. We really appreciate the breadth of expertise available at Hypha Discovery and will definitely reach out for future work."

**Director of DMPK,
US Pharma Company**

Compound	R ¹	R ²	R ³	R ⁴	R ⁵
Cyclosporin A	H	CH ₃	H	H	CH ₃
AM1	OH	CH ₃	H	H	CH ₃
AM19	OH	CH ₃	H	OH	CH ₃
AM19N	OH	CH ₃	H	H	H
AM4	H	CH ₃	OH	H	CH ₃
AM4N	H	H	H	H	CH ₃
AM49	H	CH ₃	OH	OH	CH ₃
AM4N9	H	H	H	OH	CH ₃
AM9	H	CH ₃	H	OH	CH ₃
AM9N	H	CH ₃	H	H	H



Why work with us?

High success rates. We have a high success rate in making even the most difficult-to-synthesize metabolites using our one-stop metabolite shop techniques. Our processes are applicable to broad structural types and provide a method for capturing multiple metabolites in a single screen. We also have expertise in purification and structure elucidation by NMR.

Scalable and reproducible process. We have an excellent reproducibility rate where target molecules can be scaled up to produce mg to gram quantities.

Defined timelines and costs. Metabolites are produced on a simple-fee-for-service basis, i.e. no downstream terms. The process is

stage-gated so the client has control throughout.

