

We can produce and scale-up mammalian phase I and II metabolites using microbial catalysts, mammalian tissue fractions and recombinant enzymes:

- 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-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.co.uk

Accessing metabolites of agrochemical products

Oxidised metabolites and conjugates via microbial biotransformation

Metabolites of some agrochemical products such as pesticides and herbicides possess greater plant or mammalian toxicity compared to the parent compound, thus necessitating a need for their identification, study and provision of analytical reference standards to meet regulatory requirements.

Where a synthetic route is challenging, or the identity of a metabolite is unknown, creation of metabolites by microbial biotransformation is often a successful alternative due to similarities of xenobiotic metabolism in mammals, birds, fish, soil, and to some extent, plants. Furthermore, biocatalysis affords aromatic and aliphatic site-selectivity as well as regiocontrol of aromatic hydroxylation (Kusack *et al.*, 2013).

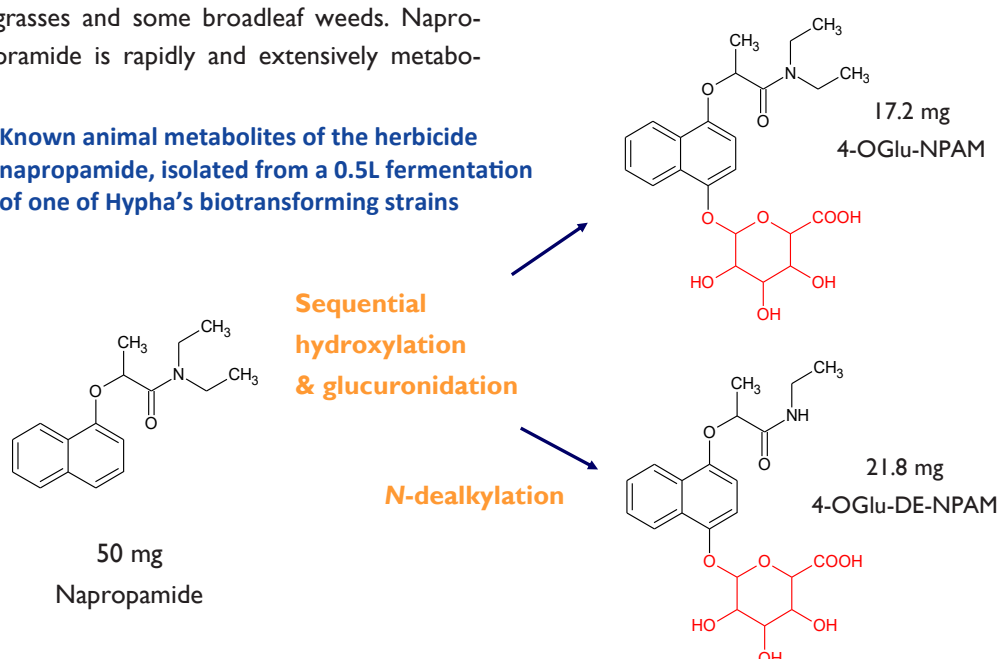
An illustrative case study was undertaken using the herbicide napropamide, effective for pre-emergence control of many annual grasses and some broadleaf weeds. Napropamide is rapidly and extensively metabo-

lized in animals, undergoing sequential hydroxylation and glucuronidation to glucuronide conjugates excreted in urine and faeces (EFSA Journal 2010, 8(4): 1565).

Napropamide was screened against several of Hypha's biotransforming strains - several hydroxylated metabolites and glucuronides were detected by LC-MS. A 0.5L fermentation of one strain with 50mg of parent compound was performed to access two of the major glucuronides relevant to animal metabolism, through sequential aromatic hydroxylation and glucuronidation with and without dealkylation. Structures were confirmed by NMR spectroscopy as those reported previously as animal metabolites (EFSA Scientific Report 2008, 140: 1-74).

Ref. Kusack *et al.*, 2013. *Bioorganic and Med. Chem. Letters* 23(20), 5471-5483.

Known animal metabolites of the herbicide napropamide, isolated from a 0.5L fermentation of one of Hypha's biotransforming strains



ABOUT HYPHA DISCOVERY

Hypha Discovery Ltd is a UK-based microbial biotechnology company providing solutions to pharmaceutical and agrochemical R&D partners through the production of mammalian and microbial metabolites, as well as specialising in microbially-derived chemicals. As part of our extensive client base, we work with 8 out of 10 of the top pharma companies and 4 out of 6 of the top agrochemical companies worldwide.