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. (Schocken, 2000). Furthermore, biocatalysis affords aromatic and aliphatic site-selectivity as well as regiocontrol of aromatic hydroxylation (Cusack et al., 2013).

In one project, Hypha produced and purified the two active hydroxylated metabolites of the neonicotinoid insecticide imidacloprid, resulting from one of two major mammalian metabolic routes. The positional isomers were separated, confirmed by NMR spectroscopy and supplied for use as analytical standards.

Mammalian metabolites of the insecticide imidacloprid, obtained via hydroxylation of the imidazoline ring by a strain from Hypha's biotransformation panel.

Known animal metabolites of the herbicide napropamide, isolated from a fermentation of one of Hypha’s biotransforming microbes

A further case study involved metabolism of the herbicide napropamide. Napropamide is rapidly and extensively metabolized in animals, undergoing sequential hydroxylation and glucuronidation prior to excretion in urine and faeces (EFSA Journal 2010, 8(4):1565). Napropamide was screened against a panel of Hypha’s biotransforming strains with several hydroxylated metabolites and glucuronides detected by LC-MS. A 0.5L scale-up biotransformation enabled access to two of the major glucuronides relevant to animal metabolism. Structures were confirmed by NMR spectroscopy as those reported previously as animal metabolites (EFSA Scientific Report 2008, 140:1-74).