

Supply of stable-labelled and radiolabelled metabolites and microbial natural products

Hypha are experts in applying microbial chemistry to provide difficult-to-synthesize human metabolites and microbial natural products

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
 N-acetylation
 Transamination

Formation and scale-up of stable and radiolabelled metabolites and natural products is possible by combining Hypha's expertise in microbial chemistry and Selcia's radiochemistry capabilities.

Labelled mammalian and agrochemical metabolites

Hypha's microbial biocatalysis process is effective at generating metabolites at up to gram scale. Through Hypha and Selcia's partnership, [¹³C], [¹⁴C], [²H], [³H] and [¹⁵N]-labelled metabolites can be accessed to support regulatory, development or research projects in the pharma and crop protection industries. Hypha establishes optimized processes using unlabelled or stable labelled parent substrates, which can then be transferred to Selcia's state-of-the-art radiochemistry labs for the production of radiolabelled metabolites.

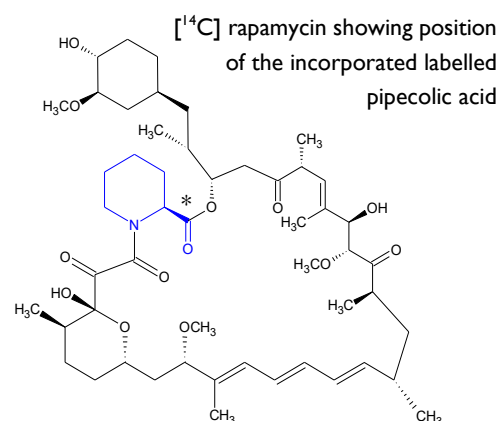
Production of ¹⁴C-labelled microbial natural products

Our combined microbial and radiochemistry expertise permits production of [¹⁴C]-enriched semi-synthetic and natural products via isotopically-labelled precursor feeding. The first step involves sourcing and fermenting the microorganism to achieve acceptable yields of the product. Incorporation of an externally fed [¹³C]-

labelled biosynthetic precursor to a fermentation is then undertaken, with confirmation of the location and extent of uptake of the [¹³C] label. The process can then be replicated in Selcia's facility to incorporate a synthesised [¹⁴C]-labelled precursor into the final natural product.

Case study— Collaborative project to supply radiolabelled rapamycin

Rapamycin is a microbial product of *Streptomyces rapamycinicus* and has potent immunosuppressive and anti-proliferative properties. Pilot work was successfully undertaken by Hypha to provide an optimised fermentation process for incorporation of [¹³C] labelled L-pipecolic acid into rapamycin. The process was then transferred to Selcia for production and purification of the [¹⁴C] labelled rapamycin from single labelled [¹⁴COOH] L-pipecolic acid, synthesised by Selcia using a short, efficient synthesis from [¹⁴C] CO₂. A total of 33mg of [¹⁴C] rapamycin was purified at Selcia with a radiochemical and chemical purity of 94%, and a specific activity of 16.3 mCi/mmol.



For more information about Hypha's services, contact mail@hyphadiscovery.co.uk or for radiolabelling enquiries, contact Selcia using contact@selcia.com

ABOUT SELCIA

Selcia is a global contract research provider of integrated drug discovery, medicinal chemistry and ¹⁴C radiolabeled compounds. Established in 2001, the company has two divisions: Selcia Drug Discovery - with medicinal chemistry, biology ADME and a unique peptidyl prolyl isomerase (PPIase) inhibitor screening platform; and Selcia Radiolabeling - one of the world's largest suppliers of custom ¹⁴C radiochemicals.

ABOUT HYPHA DISCOVERY

Hypha Discovery Ltd is a 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 microbially-derived chemicals. We work with 8 out of 10 of the top pharma companies and 4 out of 6 of the top agrochemical companies worldwide.