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HYPHA DISCOVERY

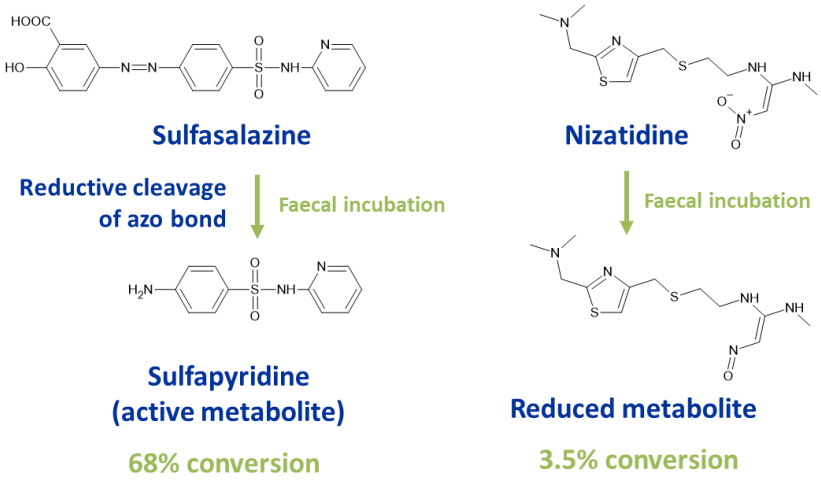
Metabolites and molecules for tomorrow's drugs

# MetID of Gut Metabolites

## Biotransformation of drugs using pooled human faecal material

### Key Features

- Human origin
- Pooled mixed sex source
- Screen and scale-up: 100s µg to mg amounts for MetID
- Purification expertise
- Structure elucidation by cryoprobe NMR




**Reductive biotransformation of sulfasalazine and nizatidine by incubation in pooled human faecal material under oxygen depleted conditions.**

Microbiota in the human gut are increasingly being considered as a virtual organ which plays a critical role in drug metabolism. The majority are obligate anaerobes from the genera *Bacteriodes, Clostridium, Lactobacillus, Escherichia* and *Bifidobacteria*, together with an assortment of other microorganisms.[1] The role of this "organ" in the metabolism of some drugs is complicated by variability in the individual composition of microbial species in the gastrointestinal tract, potentially causing differences in the drug response.

As well as activation of pro-drugs, direct microbiome-derived metabolism can lead to deactivation, reactivation through enterohepatic recycling, or biotransformation of a drug to a toxic metabolite.

## Screening service

Hypha's human faecal pool can be used to screen for reduced metabolites of drugs, as exemplified with sulfasalazine and nizatidine. In these case studies, drugs were incubated in human faecal material derived from several mixed sex donors under oxygen depleted conditions. The reduced metabolites were easily detected by LC-MS.

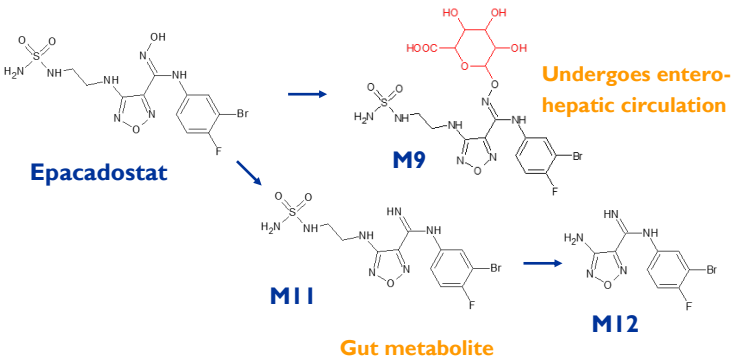
## Scalability for MetID

Human faecal incubations can be scaled up to provide material for purification of metabolites prior to structure elucidation by cryoprobe NMR.

## Projects for clients

We have undertaken a number of projects for clients where identification of a suspected gut-derived metabolite of a drug in clinical trials was needed, sometimes revealing surprising structures. These have included reduced and unusual conjugated metabolites.

A reduced metabolite of epacadostat, M11, was surprisingly found to be produced by one of Hypha's microbes under aerobic conditions. Microbial biotransformation of epacadostat also yielded a major *O*-glucuronide M9, and a metabolite M12 derived from CYP mediated metabolism of M11.[2]




***Contact us to discuss your MetID project***
**enquiries@hyphadiscovery.com**

[1]Wilson, I.D. and Nicholson, J.K, 2017. Transl Res.,179: 204–222.
[2]Boer *et al.*, 2016. Drug Metabolism and Disposition, 44 (10) 1668-1674.