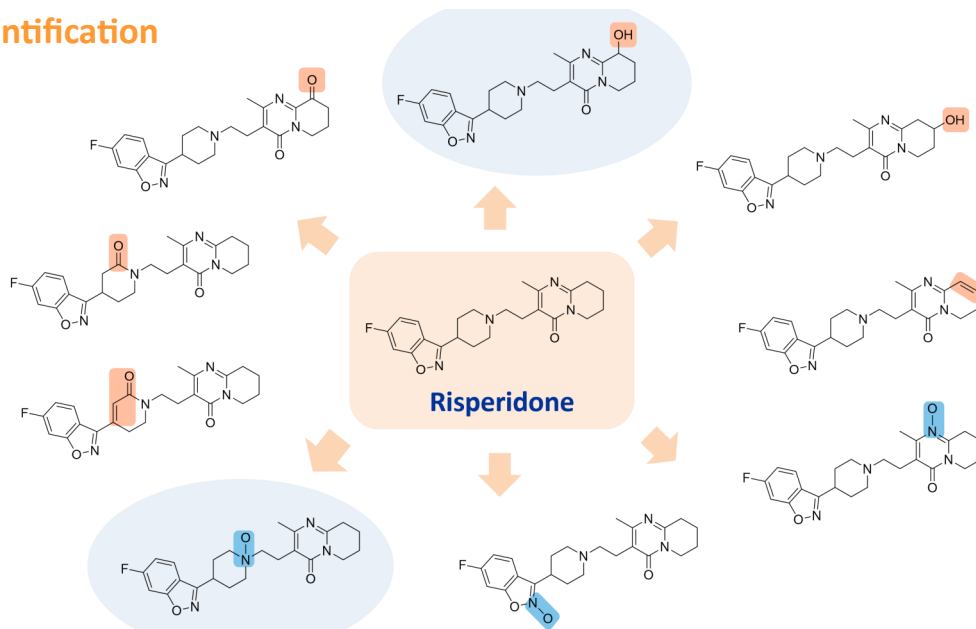


## API impurities and degradation products

### Synthesis, purification and identification

#### Services

-  Purification from complex matrices
-  Identification by cryoprobe NMR for structure identification
-  Rapid generation of diverse oxidized products to understand an API's oxidative sensitivity
-  Backed up by biotransformation options



Products of risperidone produced in Hypha's chemical oxidation screen. The two major degradation products in dosage form are shaded - an N-oxide and 9-hydroxy risperidone (also known as paliperidone, the primary active metabolite).<sup>1</sup>

The safety of a drug is impacted by its susceptibility to form degradation products. To meet regulatory guidelines, significant degradation products must be identified. This involves isolation and definitive structure elucidation of the degradate or impurity, typically by NMR spectroscopy. Purified amounts of impurities may be required for use as analytical standards, or for safety assessments.

#### A Unique Toolbox

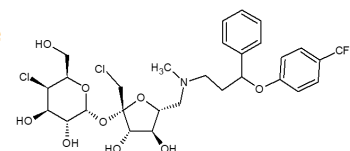
Hypha have put together a set of late stage chemical oxidation conditions, resulting in a toolbox for the synthesis and identification of degradation products. Our expertise in biotransformation and micro-purification, widens the suite of techniques to make and identify degradation products.

#### Features

- Purification from shelf life study samples, and structure elucidation by cryoprobe NMR, e.g. on ~100 micrograms
- Panel of late stage chemical oxidation conditions to synthesise mg-g amounts
- Complemented by microbial and enzymatic biotransformation

#### Identification of Fluoxetine Storage Impurities<sup>2</sup>

Hypha purified and identified two sucralose conjugates of fluoxetine, formed during a study where the drug had been stored at 50°C for 2 months. Simulation of the reaction at 50°C for 7 days permitted purification and identification of two sucralose conjugates. Subtle differences in the NMR spectra revealed the presence of stereoisomers resulting from the reaction of sucralose with racemic fluoxetine.



#### Chemical Oxidation Screen

Oxidative degradation pathways commonly result in the most complex reaction profiles, highlighted by Nanda and colleagues who state that, "...faster and practical ways of enriching an API with relevant oxidative degradates and their isolation in pure form is highly desirable."<sup>3</sup> Thus, availability of an oxidation toolkit incorporating broad chemistry is beneficial for rapidly generating oxidised products. Hypha's chemical oxidation screen creates oxidised products using 14 diverse conditions, constructed from a comprehensive evaluation of the literature and in-house knowledge. Reactions can be scaled to make gram quantities of the degradate. Multiple products can be isolated from complex mixtures and structures elucidated using cryoprobe NMR.

For more information contact us at [enquiries@hyphadiscovery.com](mailto:enquiries@hyphadiscovery.com)

<sup>1</sup> Tomar et al., 2004. Journal of Pharmaceutical and Biomedical Analysis, 36, (1), 231-235

<sup>2</sup> Work done for Neuropharm, data now owned by Herscu Laboratory.

<sup>3</sup> Nanda et al., 2019. Journal of Pharmaceutical Sciences, 108, 4, 1466-1475.