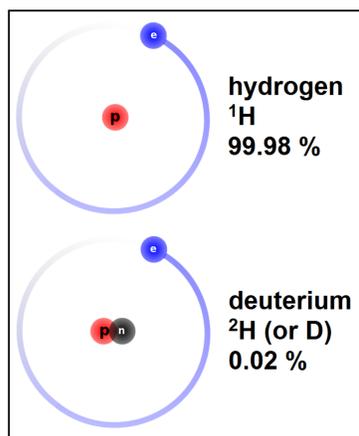


Molecular Deuteration for Clinical Agent Analogues

Tamim Darwish, Rhys Murphy, Rachel Codd



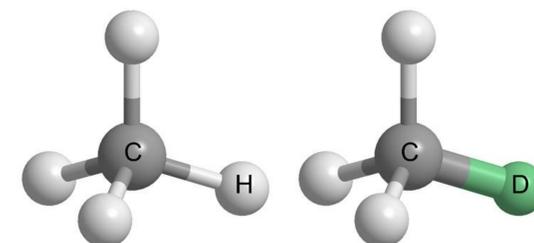
Deuterium is a stable (non-radioactive) isotope of hydrogen.

The process of switching hydrogen with deuterium is known as **deuteration**.

Incorporation of deuterium at specific locations in molecules can offset degradation, leading to improved stability and extended product lifetimes.

This occurs because the C–D bond is stronger than the C–H bond, and so molecules can become less vulnerable to heat, light, oxidation, or metabolism.

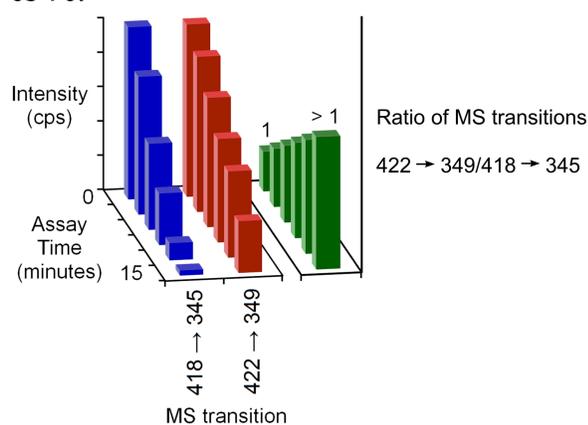
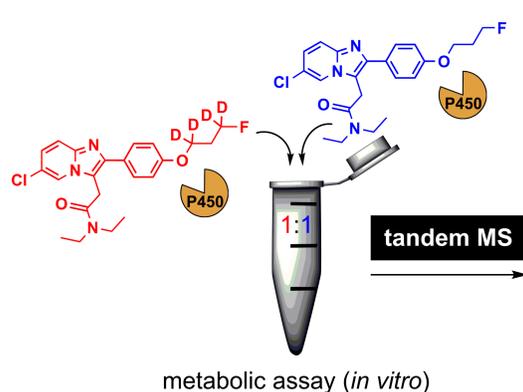
Deuteration has applications in **health, medicine, and materials science**.



The **National Deuteration Facility (NDF)** uses chemical and biological deuteration techniques to supply bespoke deuterated molecules requested by our national and international user base. We also are leading projects on **deuterated radiotracers** and other **biologically important molecules**.

Deuterated Radiotracers/Drugs

Analytica Chimica Acta, 2019, Vol. 1064, p. 65-70.



NDF collaboration with Human Health and Biosciences at ANSTO: Andrew Wotherspoon, Benjamin Fraser, Nageshwar Yepuri, Naomi Wyatt.

We have developed an **analytical method to rapidly screen for improvement in metabolic stability of deuterated drugs and biomolecules (in vitro)**.

There are significant efforts by pharmaceutical companies to improve the properties of medications by deuteration (multi-billion \$ industry).

Radiotracers are drugs used for medical imaging (e.g. PET scan) which assist in disease diagnosis and tracking disease progression.

These sometimes exhibit a short biological half life due to rapid metabolism, which can cleave the radiolabel beacon.

We have demonstrated that deuterated PBR111 (a radiotracer with potential for imaging neuroinflammation) has **improved metabolic stability (in vitro, and in vivo in rat)** and **improved medical image quality (PET scan of rat)**, compared to the non-deuterated analogue.

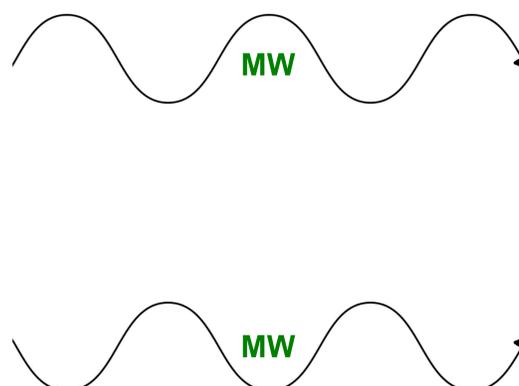
Microwave-Assisted Deuteration

The NDF has a state-of-the-art **microwave reactor**:

- high temperatures (300 °C) and pressures (190 atm).
- microwave power of 1500 W.
- reaction volumes of 10-600 mL.
- rapid cooling of reaction mixtures.

We are investigating microwave-assisted deuteration to:

- increase yields.
- increase purity.
- decrease reaction times.
- decrease degradation and/or side-products.



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