Cytochrome P450 (CYP) Inhibition

The cytochrome P450 (CYP) enzymes play a critical role in the metabolism of many drug, and alterations to the activity of these enzymes caused by co-administered drugs may lead to a metabolic drug-drug interactions (DDI). *In vitro* tools are available for early detection of potential DDI perpetrators and are an integral part of early safety assessment in the drug discovery process.

Compounds are incubated at increasing concentrations with microsomes in the presence of CYP specific substrates and enzyme co-factor at 37 °C. After the incubation, samples are quenched and analysed by LC-MS. IC_{50} is calculated using GraphPad Prism.

Standard Assay Conditions

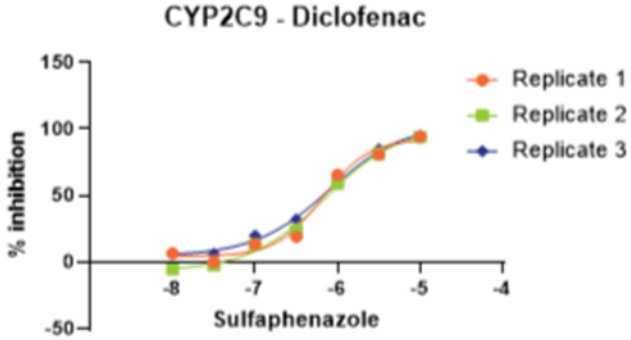
- 0.2 mg/mL human liver microsomal protein concentration
- 7 CYP isoforms available

CYP1A2	CYP2B6	CYP2C8	CYP2C9
CYP2C19	CYP2D6	CYP3A4 (Midazolam)	CYP3A4 (Testosterone)

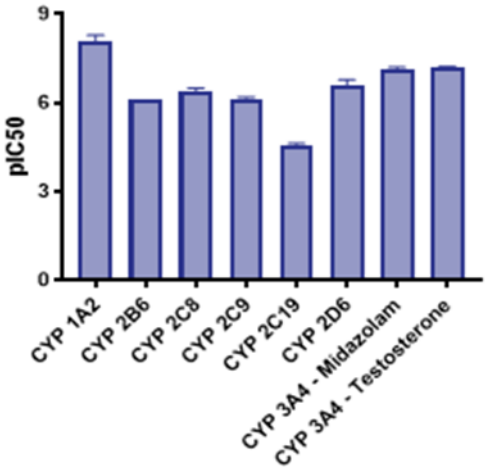
- FDA approved marker inhibitors/substrates
- 7 compound concentrations tested:
  - 0.04 – 50.00 µM
- pH 7.4 phosphate buffer
- NADPH co-factor
- 1% organic solvent final in the incubation mixture
- N=2 replicates
- Analysis by LC-MS

Compound Requirements

100 µL of a 10 mM stock or 1 mg of solid (accurately weighed to 2 decimal places)



IC_{50} curve of Sulfaphenazole (marker inhibitor compound) with Diclofenac (2C9 substrate) . % inhibition relative to solvent control. Data from three experiments; 2 replicates per experiment.



Geomean of pIC_{50} values for all isoforms. Data from three experiments.

Deliverables

Graphical representation of the inhibition curves and IC_{50} values in µM for all CYP isoforms tested.

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All our assays can be customised to answer specific project questions

Contact us for more information on standard or customised assay formats