In vitro **ADME & PK**

Monoamine Oxidase (MAO) Inhibition

Background Information

'In human brain the predominant form is MAO-B, expressed at highest levels in astrocytes and serotonergic neurons, while MAO-A is expressed at highest levels in catecholaminergic neurons.'

[1]Hotamisligil GS and Breakefield XO (1991) *Am J Hum Genet* **49(2)**; 383–392

- Monoamine oxidases (MAO) are membrane-associated enzymes located specifically to the outer mitochondrial membrane. They are the major enzymes participating in the catabolism of monoamine neurotransmitters and related exogenous amines.

- Two isoforms of MAO exist, MAO-A and MAO-B, which differ in their substrate specificity, inhibitor selectivity and tissue distribution.

- Selective MAO-A inhibitors are useful in the therapy of depression and anxiety whereas MAO-B inhibitors are often used in the treatment of Parkinson's and Alzheimer's diseases.

- Cyprotex's MAO inhibition assay identifies if your compound is an inhibitor for either MAO-A or MAO-B.

Protocol

Substrate
Kynuramine

Metabolite
4-hydroxyquinolinol

Test Article Concentrations
0, 0.4, 1, 4, 10, 40 and 100 µM
(different concentrations available)

Enzyme Source
hMAO-A and hMAO-B expressed enzymes
(Supersomes™)

Test Article Requirements
100 µL of a 40 mM DMSO solution (or equivalent amount in solid)

Positive Control
Clorgyline MAO-A
Selegiline MAO-B

Analysis Method
LC-MS/MS

Data Delivery
IC_{50}
Standard error of IC_{50}
% Control at each concentration

To find out more contact **enquiries@cyprotex.com**

Monoamine Oxidase (MAO) is a critical enzyme in the degradative deanimation of biogenic amines throughout the body[1].

Figure 1

Inhibitory specificity demonstrated for MAO-A inhibitor clorgyline using MAO-A or MAO-B expressed enzyme and kynuramine as the substrate.
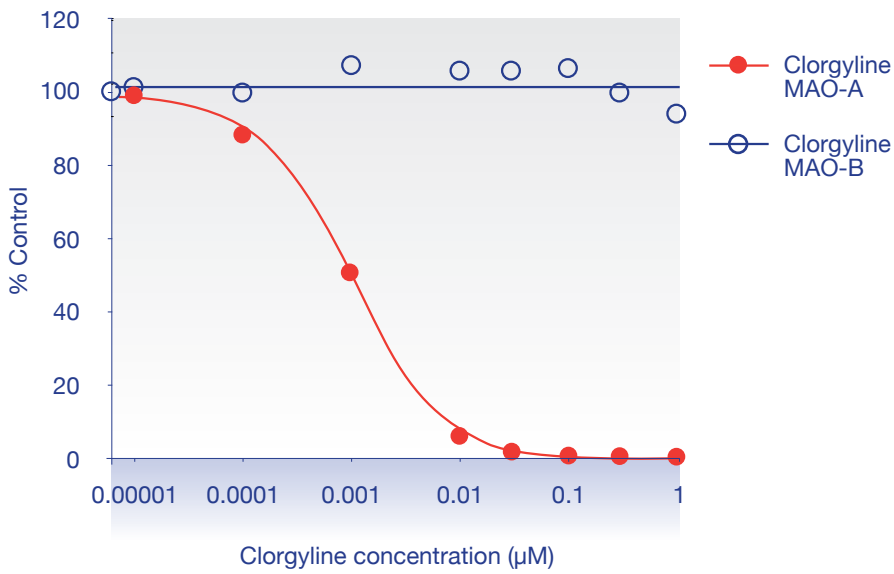
Figure 2

Inter-assay reproducibility of MAO-B inhibition using specific MAO-B inhibitor selegiline and non-specific inhibitor tranylcypromine. Each inhibitor was investigated on three separate occasions using hMAO-B expressed enzyme and kynuramine as substrate. The error bars represent the stadard error of the IC_{50} determination.
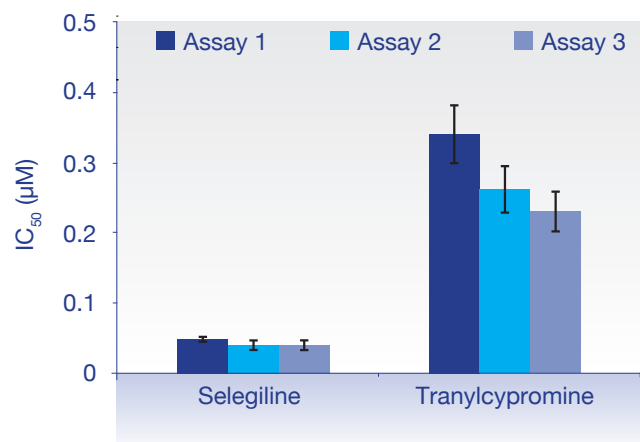
References

[1] Hotamisligil GS and Breakefield XO (1991) Human monoamine oxidase A gene determines levels of enzyme activity. *Am J Hum Genet* **49(2)**; 383-392