

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.'

¹Hotamisligil 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 μ M
(different concentrations available)

Enzyme Source

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

Test Article Requirements

100 μ L 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

IC₅₀
Standard error of IC₅₀
% Control at each concentration

Monoamine Oxidase (MAO) is a critical enzyme in the degradative deamination of biogenic amines throughout the body¹.

Figure 1

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

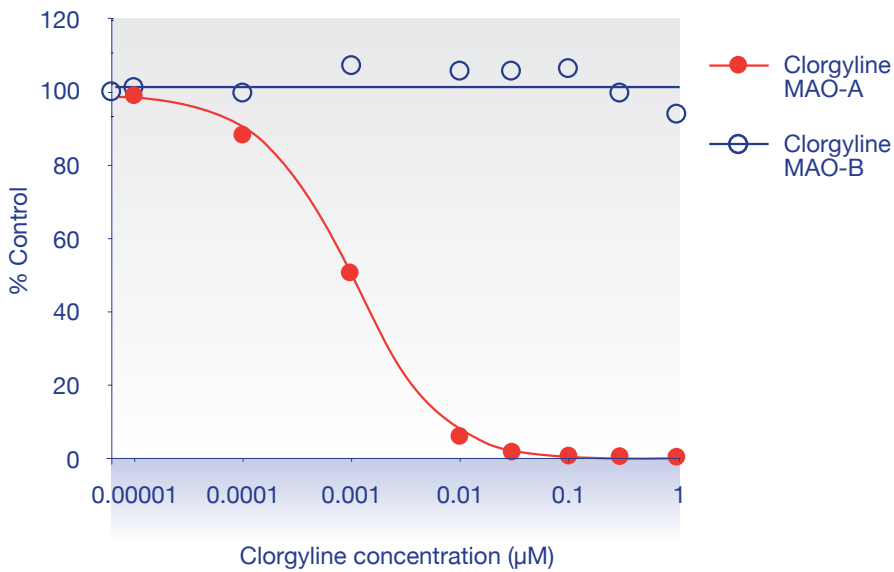
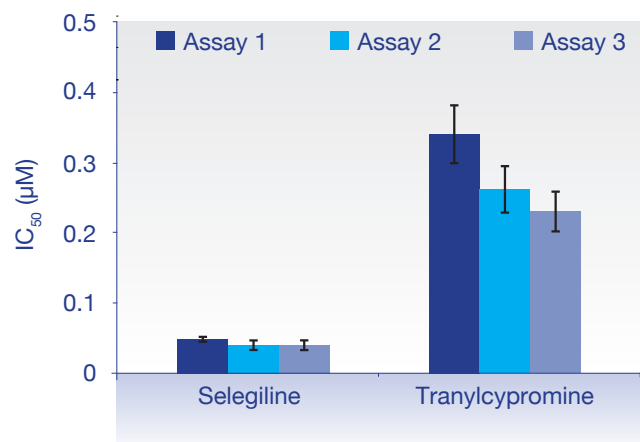


Figure 2

Inter-assay reproducibility of MAO-B inhibition using specific MAO-B inhibitor selegiline and non-specific inhibitor tranlycypromine. Each inhibitor was investigated on three separate occasions using hMAO-B expressed enzyme and kynuramine as substrate. The error bars represent the standard error of the IC₅₀ 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