**BIOLOGICAL ACTIVITY**

**Description**
LY-404187 is a potent, selective and centrally active positive allosteric modulator of AMPA receptors, with the EC$_{50}$s of 5.65, 0.15, 1.44, 1.66 and 0.21 µM for GluR1i, GluR2i, GluR2o, GluR3i and GluR4i, respectively. LY-404187 has therapeutic potential in a number of psychiatric disorders and neurodegenerative diseases[1][2].

**IC$_{50}$ & Target**
EC50: 5.65 µM (GluR1i), 0.15 µM (GluR2i), 1.44 µM (GluR2o), 1.66 µM (GluR3i), 0.21 µM (GluR4i)[2]

**In Vitro**
LY-404187 (3-10 nM) potentiates glutamate-evoked inward currents in human GluR4 transfected HEK293 cells[2].
LY-404187 (0.03-10 µM) selectively enhances glutamate-evoked currents through AMPA receptor/channels of acutely isolated pyramidal neurons with considerably greater potency (EC$_{50}$=1.3±0.3 µM) and efficacy (E$_{max}$=45.3±8.0-fold increase) [3].
LY-404187 does not affect the magnitude or time course of wholecell K$^+$ or Na$^+$ currents in pre frontal cortex (PFC) pyramidal neurons at concentrations of 10 µM[3].

**In Vivo**
LY-404187 (0.5 mg/kg; s.c for 11 days) can prevent MPTP-induced neurotoxicity in mice[4].
LY-404187 (0.5 mg/kg; s.c. for 28 days) attenuates apomorphine-induced contraversive rotations and affords significant protection against the loss of tyrosine hydroxylase positive nigral cell bodies[4].
LY-404187 (0.1 or 0.5 mg/kg; s.c. for 14 days) affords functional, neurochemical and histological protection after infusion of 6-hydroxydopamine into the substantia nigra in rats[4].
LY-404187 (0.5 mg/kg; s.c. for 14 days) delayed treatment provides functional and histological improvement, suggesting a trophic action as administration is initiated after cell death[4].
LY-404187 (0.1 and 0.5 mg/kg; s.c. for 14 days) increases GAP-43 immunoreactivity in the striatum in a dose-dependent manner[4].

**Animal Model:** Male C57BL/6J mice (20-25 g) are challenged with MPTP on day 8[4]

**Dosage:** 0.5 mg/kg

**Administration:** S.c; twice daily on weekdays and once daily at weekends for 11 days

**Result:** Attenuated the loss of tyrosine hydroxylase immunoreactivity in the substantia nigra. No significant change in tyrosine hydroxylase immunoreactivity in the dorsal and ventral striatum.
REFERENCES


