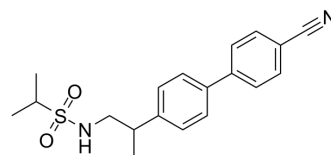


## LY-404187

<b>Cat. No.:</b>	HY-13456		
<b>CAS No.:</b>	211311-95-4		
<b>Molecular Formula:</b>	C <sub>19</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub> S		
<b>Molecular Weight:</b>	342.46		
<b>Target:</b>	iGluR		
<b>Pathway:</b>	Membrane Transporter/Ion Channel; Neuronal Signaling		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 100 mg/mL (292.00 mM; Need ultrasonic)

Solvent	Mass	Concentration		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.9200 mL	14.6002 mL	29.2005 mL
	5 mM	0.5840 mL	2.9200 mL	5.8401 mL
	10 mM	0.2920 mL	1.4600 mL	2.9200 mL

Please refer to the solubility information to select the appropriate solvent.

### BIOLOGICAL ACTIVITY

#### Description

LY-404187 is a potent, selective and centrally active positive allosteric modulator of AMPA receptors, with the EC<sub>50</sub>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<sup>[1][2]</sup>.

#### IC<sub>50</sub> & Target

EC<sub>50</sub>: 5.65 μM (GluR1i), 0.15 μM (GluR2i), 1.44 μM (GluR2o), 1.66 μM (GluR3i), 0.21 μM (GluR4i)<sup>[2]</sup>

#### In Vitro

LY-404187 (3-10 nM) potentiates glutamate-evoked inward currents in human GluR4 transfected HEK293 cells<sup>[2]</sup>.  
 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<sub>50</sub>=1.3±0.3 μM) and efficacy (E<sub>max</sub>=45.3±8.0-fold increase)<sup>[3]</sup>.  
 LY-404187 does not affect the magnitude or time course of wholecell K<sup>+</sup> or Na<sup>+</sup> currents in pre frontal cortex (PFC) pyramidal neurons at concentrations of 10 μM<sup>[3]</sup>.  
 MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

LY-404187 (0.5 mg/kg; s.c for 11 days) can prevent MPTP-induced neurotoxicity in mice<sup>[4]</sup>.

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<sup>[4]</sup>.  
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<sup>[4]</sup>.  
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<sup>[4]</sup>.  
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<sup>[4]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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

- [1]. Quirk JC, et, al. LY404187: a novel positive allosteric modulator of AMPA receptors. *CNS Drug Rev.* Fall 2002; 8(3): 255-82.
- [2]. Miu P, et, al. Novel AMPA receptor potentiators LY392098 and LY404187: effects on recombinant human AMPA receptors in vitro. *Neuropharmacology.* 2001 Jun; 40(8): 976-83.
- [3]. Baumbarger PJ, et, al. Positive modulation of alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptors in prefrontal cortical pyramidal neurons by a novel allosteric potentiator. *J Pharmacol Exp Ther.* 2001 Jul; 298(1): 86-102.
- [4]. O'Neill MJ, et, al. Neurotrophic actions of the novel AMPA receptor potentiator, LY404187, in rodent models of Parkinson's disease. *Eur J Pharmacol.* 2004 Feb 20; 486(2): 163-74.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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