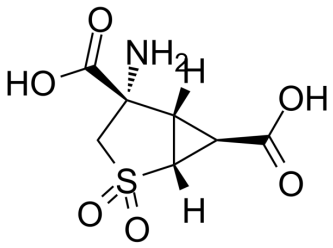
LY404039

Cat. No.:	HY-50906
CAS No.:	635318-11-5
Molecular Formula:	$C_7H_9NO_6S$
Molecular Weight:	235.21
Target:	mGluR
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

H_2O : 5.2 mg/mL (22.11 mM; ultrasonic and adjust pH to 6 with NaOH)
DMSO : 3.84 mg/mL (16.33 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.2515 mL	21.2576 mL	42.5152 mL
	5 mM	0.8503 mL	4.2515 mL	8.5030 mL
	10 mM	0.4252 mL	2.1258 mL	4.2515 mL

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

In Vivo

1. Add each solvent one by one: PBS
Solubility: 2 mg/mL (8.50 mM); Clear solution; Need ultrasonic and warming and heat to 60°C

BIOLOGICAL ACTIVITY

Description

LY404039 is a potent, selective and orally active mGluR2 and mGluR3 agonist with K_is of 149 nM and 92 nM for recombinant human mGluR2 and mGluR3, respectively. LY404039 shows >100-fold selectivity for mGluR2/3 over other receptors/transproters. LY404039 has antipsychotic and anxiolytic effects[1].

IC_{50} & Target

mGlu2 Receptor 149 nM (Ki, Recombinant human mGluR2)	hmGluR3 92 nM (Ki)

In Vitro

LY404039 is a nanomolar potent agonist in rat neurons expressing native mGlu2/3 receptors (K_i = 88 nM)[1].
Functionally, LY404039 potently inhibits Forskolin-stimulated cAMP formation in cells expressing human mGlu2 (EC_{50} = 23 nM) and mGlu3 receptors (EC_{50} = 48 nM)[1].
Electrophysiological studies indicate that LY404039 suppresses electrically evoked excitatory activity in the striatum, and

	serotonin-induced L-glutamate release in the prefrontal cortex. LY404039 suppresses the frequency of 5-HT-induced excitatory postsynaptic currents (EPSCs) with an EC_{50} of 82.3 nM and with a near maximal suppression of 85.6% at 1 μM[1]. LY404039 inhibits the binding of the D2-specific antagonist, [3H]domperidone, to the human cloned D2 receptor with dissociation constants of 8.2 nM at D2High and 1640 nM at D2Low. Using rat striatal tissue, LY404039 has dissociation constants of 12.6 nM at D2High and 2100 nM at D2Low[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	LY404039 attenuates amphetamine- and phencyclidine-induced hyperlocomotion (3-30 and 10 mg/kg, respectively). LY404039 (3-10 mg/kg) inhibits conditioned avoidance responding. LY404039 also reduces fear-potentiated startle in rats (3-30 μg/kg) and marble burying in mice (3-10 mg/kg), indicating anxiolytic-like effects. LY404039 (10 mg/kg) also increases dopamine and serotonin release/turnover in the prefrontal cortex[3]. Following oral administration of LY404039 to fasted rats at doses of 1, 3, or 10 mg/kg, exposure increased proportionally with dose. LY404039 (10 mg/kg; p.o.) treatment shows the C_{max} is 1528.5 ng/mL and T_{max} is 2 hours in rats[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- SSRN. 2023 Apr 26.

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REFERENCES

[1]. Linda M Rorick-Kehn, et al. Pharmacological and pharmacokinetic properties of a structurally novel, potent, and selective metabotropic glutamate 2/3 receptor agonist: in vitro characterization of agonist (-)-(1R,4S,5S,6S)-4-amino-2-sulfonylbicyclo[3.1.0]-

[2]. Seeman P. An agonist at glutamate and dopamine D2 receptors, LY404039. Neuropharmacology. 2013 Mar;66:87-8.

[3]. Rorick-Kehn LM, et al. In vivo pharmacological characterization of the structurally novel, potent, selective mGlu2/3 receptor agonistLY404039 in animal models of psychiatric disorders. Psychopharmacology (Berl). 2007 Jul;193(1):121-36.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA