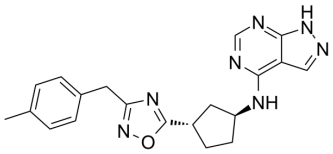
NMDA receptor antagonist 2

Cat. No.:	HY-136459
CAS No.:	875898-41-2
Molecular Formula:	$C_{20}H_{21}N_7O$
Molecular Weight:	375.43
Target:	iGluR
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	NMDA receptor antagonist 2 is a potent and orally active NR2B subtype-selective NMDA antagonist with an IC_{50} and a K_i of 1.0 nM and 0.88 nM, respectively. NMDA receptor antagonist 2 is used for the study of neuropathic pain and Parkinson's disease[1].
IC_{50} & Target	IC50: 1.0 nM; Ki: 0.88 nM (NR2B subtype NMDA)[1]
In Vitro	NMDA receptor antagonist 2 leads to excellent potency at NR2B (K_i=0.88 nM) and selectivity over hERG binding (IP=20000 nM). NMDA receptor antagonist 2 is evaluated in a functional assay measuring Ca_{2+} flux in cells expressing recombinant NR1/NR2B receptors. Selectivity over the hERG-channel is evaluated in an MK-499-binding assay[1]. NMDA receptor antagonist 2 is highly potent in a functional assay using cells expressing NR2B (IC_{50}=1.0 nM) and remains equipotent in a binding assay using a sample of homogenized human temporal cortex (K_i=0.81 nM). In an electrophysiology assay using NR2B receptors, Compound 22 shows full blockade of ion flux with K_D=0.35 nM. Compound 22 also exhibits high levels of selectivity over NR2A (IC_{50}=200 μM), hERG binding (IP=20 μM), α-adrenergic receptors based on Prazosin binding (IC_{50}>100 μM), and CYP P450s including CYP3A4, 2C9, and 2D6[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In pharmacokinetic studies with higher species, NMDA receptor antagonist 2 shows excellent oral bioavailability (F=83%), half-life ($T_{1/2}$=7.5 hours) and clearance (CL=3.6 mL/min/kg) in dog. And it exhibits moderate clearance (CL=12 mL/min/kg) and oral bioavailability (F=17%) in rhesus, the half-life ($T_{1/2}$) is 1.5 hours[1]. In a rat pharmacokinetic study, NMDA receptor antagonist 2 shows oral bioavailability (F=23 %), half-life ($T_{1/2}$=0.7 hours) and clearance (CL=24 mL/min/kg), the receptor occupancy ED_{50} with oral administration is 4.8 mg/kg in rat[1]. In the spinal nerve ligation model of neuropathic pain in rats, surgical ligation of two lumbar nerves in the spinal column induces a state of mechanical allodynia[1]. NMDA receptor antagonist 2 (oral administration; 3-30 mg/kg) inhibits tactile allodynia in a dose-dependent manner after oral administration at 10 and 30 mg/kg. It produces an average improvement in the maximal possible effect of 15% (3 mg/kg), 41% (10 mg/kg), and 69% (30 mg/kg) compared to vehicle treated animals[1]. NMDA receptor antagonist 2 (oral administration; 3-30 mg/kg) is efficacious in an acute rodent model of Parkinson's disease. Haloperidol (HY-14538) is administered at a dose previously shown to elicit an acute cataleptic response in rats, compound 22 reduces catalepsy scores in a dose-dependent manner, producing average improvements of 34% (3 mg/kg), 86% (10 mg/kg), and 92% (30 mg/kg) when it compares to vehicle group[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Mark E Layton, et al. Discovery of 3-substituted Aminocyclopentanes as Potent and Orally Bioavailable NR2B Subtype-Selective NMDA Antagonists.

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