NP10679

Cat. No.: HY-148825

Molecular Formula: $C_{23}H_{26}F_3N_3O_3$

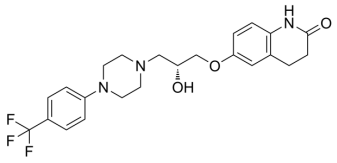
Molecular Weight: 449.47

Target: iGluR; Histamine Receptor; Potassium Channel; Cytochrome P450; Adrenergic Receptor

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling; GPCR/G Protein; Immunology/Inflammation; Metabolic Enzyme/Protease

Storage:

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 (222.48 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2248 mL	11.1242 mL	22.2484 mL
	5 mM	0.4450 mL	2.2248 mL	4.4497 mL
	10 mM	0.2225 mL	1.1124 mL	2.2248 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (5.56 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.56 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.56 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

NP10679 is a selective, pH dependent GluN2B subunit-specific N-methyl-D-aspartate (NMDA) receptor inhibitor with high oral bioavailability and good brain penetration. NP10679 inhibits GluN2B with IC_{50}s of 23 and 142 nM at pH 6.9 and 7.6, respectively. NP10679 is a histamine H1 antagonist and a hERG channel inhibitor with IC_{50}s of 73 and 620 nM, respectively. NP10679 is a reversible inhibitor of human liver CYP enzymes[1].

IC_{50} & Target				
	H_1 Receptor 0.073 μM (IC_{50})	H_1 Receptor 0.04 μM (Ki)	Alpha-1A adrenergic receptor	Alpha-1A adrenergic receptor

			0.154 μM (IC_{50})	0.603 μM (Ki)
	Alpha-1B adrenergic receptor 1.92 μM (Ki)	Alpha-1D adrenergic receptor 0.495 μM (Ki)	Alpha-2C adrenergic receptor 3.09 μM (Ki)	

In Vitro

NP10679 (1-1000 nM) shows pH-dependently effects to GluN2B with IC_{50}s of 23 and 142 nM at pH 6.9 and 7.6, respectively[2].
NP10679 shows functional inhibition to 5-HT2A, α adrenergic receptor-1A (α1A), H1-histamine receptor (H1) and hERG channel with IC_{50} values of 1.71, 0.154, 0.073 and 0.617 μM, respectively[2].
NP10679 shows K_i values of 2.29, 0.638, 1.92, 0.603, 1.92, 0.495, 3.09, 0.040 and 0.135 for 5-HT1D, 5-HT2A, 5-HT2B, α1A, α1B, α1D, α2C, H1 and serotonin transporter SERT[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

NP10679 (2, 5 and 10 mg/kg; i.p., prior to transient ischemia) reduces infarct volumes of transient ischemia mice[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57BL/6 middle cerebral artery occlusion (MCAo) model of transient ischemia mice[2]
Dosage:	2, 5 and 10 mg/kg
Administration:	Intraperitoneal injection; 2, 5 and 10 mg/kg, 15 minutes prior to transient ischemia
Result:	Dose-dependently reduced infarct volumes with an ED_{50} of 1 mg/kg.

REFERENCES

[1]. Zaczek R, et al. Phase 1 Clinical Results for NP10679, a pH-sensitive GluN2B-selective N-methyl-d-aspartate Receptor Inhibitor. Clin Pharmacol Drug Dev. 2023 Jan 15.

[2]. Myers SJ, et al. A Glutamate N-Methyl-d-Aspartate (NMDA) Receptor Subunit 2B-Selective Inhibitor of NMDA Receptor Function with Enhanced Potency at Acidic pH and Oral Bioavailability for Clinical Use. J Pharmacol Exp Ther. 2021 Oct;379(1):41-52.

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