A-582941 dihydrochloride

Cat. No.: HY-59201A

CAS No.: 848591-90-2

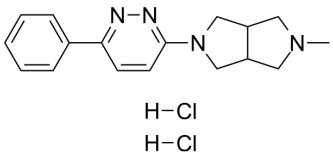
Molecular Formula: $C_{17}H_{22}Cl_2N_4$

Molecular Weight: 353.29

Target: nAChR; 5-HT Receptor

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling; GPCR/G Protein

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (283.05 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8305 mL	14.1527 mL	28.3054 mL
	5 mM	0.5661 mL	2.8305 mL	5.6611 mL
	10 mM	0.2831 mL	1.4153 mL	2.8305 mL

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

BIOLOGICAL ACTIVITY

Description

A-582941 dihydrochloride is a potent, selective and brain-penetrant partial agonist of α7 nAChR, with K_is of 10.8 and 16.7 nM in rat brain membranes and human frontal cortex, respectively. A-582941 dihydrochloride also binds to human 5-HT_3 receptor with a K_i of 150 nM. A-582941 has the potential for cognitive deficits associated with various neurodegenerative and psychiatric disorders research[1][2].

IC_{50} & Target

α7 nAChR 10.8 nM (Ki, for rat α7 receptors)	α7 nAChR 16.7 nM (Ki, for human α7 receptors)	5-HT_3 Receptor 150 nM (Ki)

In Vitro

A-582941 (0.1-100 μM) protects against cell death induced by NGF withdrawal in PC12 cells[2].
A-582941 (100 nM) increases the number of inhibitory postsynaptic potentials (IPSCs) by 260±70%, the sum of amplitudes by 220±30%, and the sum of areas by 210±40%[2].
A-582941 increases ERK1/2 phosphorylation with an EC_{50} of 95 nM in PC12 cells[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

A-582941 (3 μM/kg, i.p. once daily for 3 d) induces a moderate increase in ACh release in the medial prefrontal cortex (mPFCx) of freely moving rats[2].

A-582941 (0.01-1.00 μM/kg, i.p.) produces a dose-dependent increase in ERK1/2 phosphorylation in the cingulate cortex and hippocampus, and increases cAMP response element-binding protein (CREB) phosphorylation in the cingulate cortex in mice[2].

A-582941 (0.1-1.0 μM/kg, i.p.) evokes dose-dependent increases in Ser-9 GSK-3β phosphorylation in the mouse cingulate cortex[2].

A-582941 shows high oral bioavailability (mouse ~100%, rat 90%, dog 22%, monkey 50%) and C_{max} (mouse 18, rat 114, dog 79, monkey 39 ng/mL) following oral administration (mouse 1.0, rat 6.2, dog 3.0, monkey 3.0 μM/kg)[2].

A-582941 shows terminal elimination half-lives (mouse 1.4, rat 1.5, dog 1.4, monkey 2.0 h), plasma clearance (mouse 7.9, rat 4.7, dog 5.3, monkey 1.6 L/h/kg) and volumes of distribution (mouse 11.4, rat 9.2, dog 7.9, monkey 3.9 L/kg) following intravenous administration (mouse 1.0, rat 6.2, dog 0.5, monkey 0.5 μM/kg)[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague-Dawley CD rats (250-275 g)[2]
Dosage:	3 μM/kg
Administration:	I.p. once daily for 3 days
Result:	Increased the releases of Ach. The effect remained stable after the second and third administration.

REFERENCES

[1]. Anderson DJ, et, al. [3H]A-585539 [(1S,4S)-2,2-dimethyl-5-(6-phenylpyridazin-3-yl)-5-aza-2-azoniabicyclo[2.2.1]heptane], a novel high-affinity alpha7 neuronal nicotinic receptor agonist: radioligand binding characterization to rat and human brain. J Pharmacol Exp Ther. 2008 Jan; 324(1): 179-87.

[2]. Tietje KR, et, al. Preclinical characterization of A-582941: a novel alpha7 neuronal nicotinic receptor agonist with broad spectrum cognition-enhancing properties. CNS Neurosci Ther. Spring 2008; 14(1): 65-82.

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

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