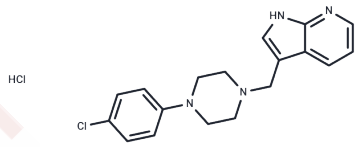
Data Sheet (Cat.No.T11799)

TargetMol

L-745870 hydrochloride

Chemical Properties



CAS No. :	1173023-36-3
Formula:	C18H20Cl2N4
Molecular Weight:	363.28
Storage:	Powder: -20°C for 3 years | In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.

Biological Description

Description	L-745870 hydrochloride has excellent brain penetration. L-745870 hydrochloride is a high-affinity, selective and orally active human dopamine D4 receptor antagonist with a Ki of 0.43 nM, and considerably weaker D2 receptor affinity with a Ki of 960 nM and D3 receptor affinity with a Ki of 2300 nM.
Targets(IC50)	Dopamine Receptor
In vitro	In vitro pharmacological studies revealed that L-745870 is an antagonist at human D4 receptors, in that L-745870 antagonized the ability of D4 receptors to inhibit agonist-induced stimulation of [35S]-GTPgS binding,?blocked the inhibition of forskolin-stimulated adenylate cyclase activity in transfected human embryonic kidney (HEK293) and Chinese hamster ovary (CHO) cells,?blocked dopamine-induced inhibition of Ca2+ currents in transfected GH4C1 pituitary cells,?inhibited D4 activation of cloned G protein-coupled inwardly rectifying K+ channels,?and antagonized dopamine-induced stimulation of extracellular acidification in transfected cells[1].
In vivo	L-745870 exhibits favorable pharmacokinetic properties (20-60% oral bioavailability and plasma t1/2 of 2.1-2.8 hours) in both rats and monkeys, with excellent brain penetration and high brain-to-plasma ratios in rats[1]. Evaluation of L-745870 in surrogate marker assays indicates that it is readily available for biological activity in the brain and at doses of 5 to 60 mg/kg p.o., it would occupy 50% of D4 receptors in the brain. L-745870 does not affect apomorphine-induced stereotypy in rats but induces catalepsy in mice at a high dose of 100 mg/kg p.o., likely due to D2 receptor occupancy. Higher doses of L-745870 are anticipated to cause extrapyramidal symptoms in primates as these CNS levels would antagonize D2 receptors. In squirrel monkeys, L-745870 (10 mg/kg p.o.) induces mild sedation and at 30 mg/kg, it causes noticeable extrapyramidal motor symptoms, notably bradykinesia[1].

Solubility Information

Solubility	DMSO: 55 mg/mL (151.4 mM),Sonication is recommended. 0.1 M HCl: 20 mg/mL (55.05 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.7527 mL	13.7635 mL	27.527 mL
5 mM	0.5505 mL	2.7527 mL	5.5054 mL
10 mM	0.2753 mL	1.3763 mL	2.7527 mL
50 mM	0.0551 mL	0.2753 mL	0.5505 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Bristow LJ, et al. Schizophrenia and L-745,870, a novel dopamine D4 receptor antagonist. Trends Pharmacol Sci. 1997 Jun;18(6):186-8.
Patel S, et al. Biological profile of L-745,870, a selective antagonist with high affinity for the dopamine D4 receptor. J Pharmacol Exp Ther. 1997 Nov;283(2):636-47.
Kulagowski JJ, et al. 3-((4-(4-Chlorophenyl)piperazin-1-yl)-methyl)-1H-pyrrolo-2,3-b-pyridine: an antagonist with high affinity and selectivity for the human dopamine D4 receptor. J Med Chem. 1996 May 10;39(10):1941-2.