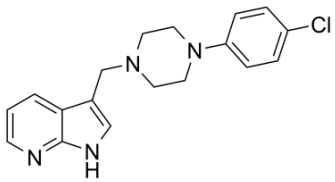
L-745870

Cat. No.:	HY-14325
CAS No.:	158985-00-3
Molecular Formula:	$C_{18}H_{19}ClN_4$
Molecular Weight:	326.82
Target:	Dopamine Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



BIOLOGICAL ACTIVITY

Description	L-745870 is a potent, selective, brain-penetrant and orally active dopamine D_4 receptor antagonist with a K_i of 0.43 nM. L-745870 shows weaker affinity for D_2 (K_i of 960 nM) and D_3 (K_i of 2300 nM) receptors, and exhibits moderate affinity for 5-HT_2 receptors, sigma sites and α-adrenoceptors[1][2][3].		
IC_{50} & Target	Human D_4 Receptor 4.3 nM (Ki)	D_2 Receptor 960 nM (Ki)	D_3 Receptor 2300 nM (Ki)
In Vitro	L-745870 is capable of antagonizing the ability of D_4 receptors to inhibit agonist-induced stimulation of [^{35}S]-GTPgS binding; blocking the inhibition of forskolin-stimulated adenylate cyclase activity in transfected human embryonic kidney (HEK293) and Chinese hamster ovary (CHO) cells; blocking dopamine-induced inhibition of Ca^{2+} currents in transfected GH4C1 pituitary cells; inhibiting D_4 activation of cloned G protein-coupled inwardly rectifying K^+ channels; and antagonizing dopamine-induced stimulation of extracellular acidification in transfected cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		
In Vivo	L-745870 has good pharmacokinetic properties (20-60% oral bioavailability and plasma $t_{1/2}$ 2.1-2.8 hours) in both rat and monkey, and excellent brain penetration with high brain to plasma ratios in rat[2]. Following oral administration to squirrel monkeys, L745870 (10 mg/kg p.o.) induces mild sedation and extrapyramidal motor symptoms, notably bradykinesia, became apparent at 30 mg/kg. Lower doses of L-745870 has no observable behavioural effects in monkeys[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		

REFERENCES

[1]. Bristow LJ, et al. Schizophrenia and L-745,870, a novel dopamine D4 receptor antagonist. Trends Pharmacol Sci. 1997 Jun;18(6):186-8.

[2]. 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.

[3]. 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.

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

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