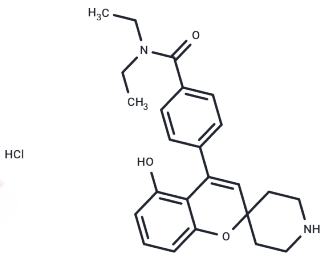
Data Sheet (Cat.No.T6175)

TargetMol

ADL-5859

Chemical Properties



CAS No. :	850173-95-4
Formula:	C24H28N2O3·HCl
Molecular Weight:	428.95
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	ADL-5859 (ADL5859 Hydrochloride) is a selective δ-opioid receptor agonist (Ki: 0.8 nM), selectivity against opioid receptor κ, μ, and little inhibition for the hERG channel.
Targets(IC50)	Opioid Receptor,Cytochromes P450,Potassium Channel
In vitro	ADL5859 agonizes δ-opioid receptor with a 1000-fold selectivity than μ- or κ-opioid receptor with Ki of 32 nM and 37 nM, respectively.ADL5859 displays weak inhibitory activity at the hERG channel with an IC50 of 78 μM. The EC50 of ADL5859 against δ opioid receptor is 20 nM.[1]
In vivo	At the screening dose of 3 mg/kg p.o., ADL5859 produces 100% reversal of hyperalgesia in the inflamed paw. The oral ED50 of ADL5859 in the FCA mechanical hyperalgesia assay is 1.4 mg/kg. The antihyperalgesia produced by ADL5859 (3 mg/kg, p.o.) is reversed by pretreatment with the δ opioid antagonist naltrindole (0.3 mg/kg s.c.), thus demonstrating a δ receptor mediated effect.In the rat forced swim assay, ADL5859 (3 mg/kg p.o.) produces robust antidepressant-like activity, as evidenced by a significant decrease in the time spent immobile and a significant increase in the time spent swimming. The bioavailability of ADL5859 (3 mg/kg p.o.) in rats and dogs is 33% and 66%, respectively.[1]ADL5859 efficiently reduces inflammatory and neuropathic pain mainly by recruiting δ-opioid receptors expressed by peripheral Nav1.8-expressing neurons.[2]
Cell Research	Membrane preparations from Chinese hamster ovary (CHO) cells stably expressing human κ, μ, or δ opioid receptors are prepared. The assay buffer used is composed of 50 mMtris(hydroxymethyl) aminomethaneHCl, pH 7.8, 1.0 mM ethylene glycol bis(β-aminoethyl ether)-N,N,N',N'-tetraacetic acid (EGTA free acid), 5.0 mM MgCl2 10 mg/L leupeptin, 10 mg/L pepstatin A, 200 mg/L bacitracin, and 0.5 mg/L aprotinin. After dilution in assay buffer and homogenization in a Polytron homogenizer for 30 seconds, membrane proteins (10-80 μg) in 250 μL of assay buffer are added to mixtures containing ADL5859 and [3H]diprenorphine (0.5-1.0 nM, 25000-50000 dpm) in 250 μL of assay buffer in 96-well deep-well polystyrene titer plates and incubated at room temperature for 60 minutes. Reactions are terminated by vacuum filtration with a Brandel MPXR-96T harvester through GF/B filters that have been pretreated with a solution of 0.5% polyethylenimine and 0.1% bovine serum albumin for at least 1 hour. The filters arewashed four times with 1.0 mL each of ice-cold 50 mM Tris-HCl, pH 7.8, and 30 μL of Microscint-20 is added to each filter. Radioactivity on the filters is

Cell Research	determined by scintillation spectrometry in a Packard TopCount. [3H]Diprenorphine with a specific activity of 50 Ci/mmolisused. The Kd values for [3H]diprenorphine binding are 0.33 nM for the κ and μ receptors and 0.26 nM for the δ receptor. Receptor expression levels, determined as Bmax values from Scatchard analyses, are 4400, 4700, and 2100 fmol/mg of protein for the κ, μ, and δ receptors, respectively. Preliminary experiments are performed to show that no specific binding is lost during the wash of the filters, that binding achieved equilibrium within the incubation time and remained at equilibrium for at least an additional 60 minutes, and that binding is linear with regard to protein concentration. Nonspecific binding, determined in the presence of 10 μM unlabeled naloxone, is less than 10% of total binding.Protein is quantified by the method of Bradford. The data from competition experiments are fit by nonlinear regression analysis with the program Prism using the four-parameter equation for one-site competition, and Ki values are subsequently calculated from EC50 values by the Cheng-Prusoff equation.(Only for Reference)

Solubility Information

Solubility	H2O: 5 mg/mL (11.66 mM),Sonication is recommended. DMSO: 35 mg/mL (81.59 mM),Sonication is recommended. Ethanol: 1 mg/mL (2.33 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 2 mg/mL (4.66 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3313 mL	11.6564 mL	23.3127 mL
5 mM	0.4663 mL	2.3313 mL	4.6625 mL
10 mM	0.2331 mL	1.1656 mL	2.3313 mL
50 mM	0.0466 mL	0.2331 mL	0.4663 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

Le Bourdonnec B, et al. J Med Chem, 2008, 51(19), 5893-5896.
Cheng L, Miao Z, Liu S, et al.Cryo-EM structure of small-molecule agonist bound delta opioid receptor-Gi complex enables discovery of biased compound.Nature Communications.2024, 15(1): 8284.
Nozaki C, et al. J Pharmacol Exp Ther, 2012, 342(3), 799-807.

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