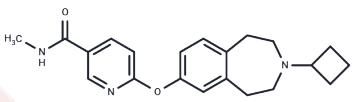
Data Sheet (Cat.No.TQ0066)

TargetMol

GSK189254A

Chemical Properties



CAS No. : 720690-73-3

Formula: C21H25N3O2

Molecular Weight: 351.44

Storage: Store at low temperature
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	GSK189254A (GSK189254) is a potent and specific histamine H3 receptor antagonist (pKi values: 9.59-9.90 and 8.51-9.17 for human and rat H3).
Targets(IC50)	Histamine Receptor
In vitro	GSK189254 has a high affinity for both recombinant H3 receptors expressed in HEK-293-MSR-II cells and native H3 receptors expressed in the cerebral cortex of several species. GSK189254 generally exhibits a higher affinity for human and pig H3 receptors compared with mouse, rat, and dog H3 receptors. GSK189254 may have therapeutic potential for the symptomatic treatment of dementia in Alzheimer's disease and other cognitive disorders [1].
In vivo	In both Ox+/+ and Ox?/? mice, acute GSK189254 administration effectively increases wakefulness and reduces both slow wave and paradoxical sleep comparably to modafinil, additionally decreasing narcoleptic episodes in Ox?/? mice [2]. At doses ranging from 0.3 to 3 mg/kg administered orally, GSK189254 enhances the release of acetylcholine, noradrenaline, and dopamine in the anterior cingulate cortex, and elevates acetylcholine levels in the dorsal hippocampus. Significantly, GSK189254 enhances rats' cognitive performance across various paradigms, including passive avoidance, water maze, object recognition, and attentional set shift tasks [1].
Animal Research	Pharmacokinetic studies with GSK189254 are conducted in conscious male Sprague-Dawley rats. Animals receive an intravenous infusion of GSK189254 (n=3) administered at a nominal dose level of 1 mg of free base/kg for 1 h via the femoral vein cannula (10 mL/h/kg). GSK189254 is dissolved in 0.9% (w/v) saline at a target concentration of 0.1 mg free base/mL and filtered with a 0.22-mm Millex-GV filter before administration. After an ish out of at least 2 days, the same rats received a single oral administration of GSK189254 by gastric gavage to achieve a target dose of 2 mg of free base/kg. GSK189254 is formulated in 1% (w/v) aqueous methylcellulose at a target concentration of 0.4 mg free base/mL [1]. The vehicle consists of 0.05 mL NaCl at 0.9% containing methylcellulose at 1%. GSK189254 is a dissolved in-vehicle solution. The effects of acute and repeat administration of GSK189254 on the sleep-wake cycle in wild-type (Ox+/+) and orexin knockout (Ox?/?) mice is investigated. GSK189254 (3 and 10 mg/kg, p.o.) is administered on the sleep-wake cycle in Ox+/+ and Ox?/? mice, dosed at 10 h. The oral administration dose of GSK189254 is 10 mg/kg [2].

Solubility Information

Solubility	DMSO: 24 mg/mL (68.29 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 (5.69 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	2.8454 mL	14.2272 mL	28.4544 mL
5 mM	0.5691 mL	2.8454 mL	5.6909 mL
10 mM	0.2845 mL	1.4227 mL	2.8454 mL
50 mM	0.0569 mL	0.2845 mL	0.5691 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

Medhurst AD, et al. GSK189254, a novel H3 receptor antagonist that binds to histamine H3 receptors in Alzheimer's disease brain and improves cognitive performance in preclinical models. J Pharmacol Exp Ther. 2007 Jun;321(3):1032-45.

Guo RX, et al. Differential effects of acute and repeat dosing with the H3 antagonist GSK189254 on the sleep-wake cycle and narcoleptic episodes in Ox-/- mice.Br J Pharmacol. 2009 May;157(1):104-17.