GSK189254A

Cat. No.: HY-14111

CAS No.: 720690-73-3

Molecular Formula: $C_{21}H_{25}N_3O_2$

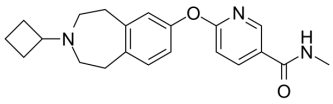
Molecular Weight: 351.44

Target: Histamine Receptor

Pathway: GPCR/G Protein; Immunology/Inflammation; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (71.14 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.11 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.11 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK189254A (GSK189254) is a novel, potent and selective histamine H3 receptor antagonist with pK_i values of 9.59-9.90 and 8.51-9.17 for human and rat H3, respectively.

IC_{50} & Target

pKi: 9.59-9.90 (H3, human), 8.51-9.17 (H3, rat)[1]

In Vitro

GSK189254 has 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 higher affinity for human and pig H3

	receptors compared with rat,mouse, and dog H3 receptors. [^{3}H]GSK189254 binds in rat and human brain areas, including cortex and hippocampus. GSK189254 may have therapeutic potential for the symptomatic treatment of dementia in Alzheimer's disease and other cognitive disorders [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GSK189254 (0.3-3 mg/kg p.o.) increases the release of acetylcholine, noradrenaline, and dopamine in the anterior cingulate cortex and acetylcholine in the dorsal hippocampus. GSK189254 significantly improves performance of rats in diverse cognition paradigms, including passive avoidance, water maze, object recognition, and attentional set shift[1]. In Ox+/+ and Ox−/− mice, acute administration of GSK189254 increases W and decreases slow wave and paradoxical sleep to a similar degree to modafinil, while it reduces narcoleptic episodes in Ox−/− mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1][2]	Rats: Pharmacokinetic studies with GSK189254 are conducted in conscious male Sprague-Dawley rats. Animals receives 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 a 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]. Mice: The vehicle consists of 0.05 mL NaCl at 0.9% containing methylcellulose at 1%. GSK189254 is 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Int J Mol Sci. 2022, 23(22), 14314

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REFERENCES

[1]. 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.

[2]. 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.

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