Samelisant

Cat. No.: HY-120124

CAS No.: 1394808-20-8

Molecular Formula: $C_{21}H_{33}Cl_2N_3O_3$

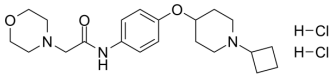
Molecular Weight: 446.41

Target: Histamine Receptor

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

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 62.5 mg/mL (140.01 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2401 mL	11.2005 mL	22.4009 mL
	5 mM	0.4480 mL	2.2401 mL	4.4802 mL
	10 mM	0.2240 mL	1.1200 mL	2.2401 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: ≥ 2.08 mg/mL (4.66 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.66 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.66 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Samelisant (SUVN-G3031) is a potent and selective histamine H3 receptor (H3R) inverse agonist with good brain penetration and oral bioavailability. Samelisant has a similar binding affinity towards human (hH3R; K_i=8.7 nM) and rat (rH3R;K_i=9.8 nM) H3R indicating no inter-species differences. Samelisant can be used for the research of sleep-related disorders[1].

In Vitro

Samelisant displays inverse agonist activity and it exhibits very high selectivity towards H3R. The pEC_{50} value of histamine (8.5) for human H3 receptor increases to 8.2, 7.3 and 6.2 after treatment with 1, 10 and 100 nM of Samelisant, respectively. The pEC_{50} value of histamine (8.2) for rat H3 receptor increases to 7.9, 7.4 and 6.4 after treatment with 1, 10 and 100 nmol/L of Samelisant, respectively[1].

	Samelisant binds to the orthosteric site in a reversible manner with K_b values of 1.3 nM and 1.1 nM deduced from pA_2 value for human and rat H3R, respectively[1]. Samelisant also modulates dopamine and norepinephrine levels in the cerebral cortex while it has no effects on dopamine levels in the striatum or nucleus accumbens[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Treatment with Samelisant (10 and 30 mg/kg, p.o.) produces a significant increase in wakefulness with a concomitant decrease in non-rapid eye movement sleep (NREM) sleep in orexin knockout mice subjected to sleep electroencephalography (EEG)[1]. Samelisant also produces a significant decrease in direct rapid eye movement (REM) sleep onset (DREM) episodes, demonstrating its anticataplectic effects in an animal model relevant to narcolepsy[1]. Samelisant treatment in mice produces a dose-dependent increase in tele-methylhistamine levels indicating the activation of histaminergic neurotransmission[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Wistar rats or male C57BL6J mice[1]
Dosage:	1, 3, 10, and 30 mg/kg
Administration:	Oral administration
Result:	Produced a dose-dependent increase in t-MH levels in the frontal cortex, hypothalamus and cerebrospinal fluid (CSF) of male Wistar rats.Produced a significant increase in t-MH levels of the frontal cortex, striatum and hypothalamus in mice.

REFERENCES

[1]. Ramakrishna Nirogi, et al. Samelisant (SUVN-G3031), a potent, selective and orally active histamine H3 receptor inverse agonist for the potential treatment of narcolepsy: pharmacological and neurochemical characterisation. Psychopharmacology (Berl). 2021 Jun;238(6):1495-1511.

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