Samelisant free base

Cat. No.: HY-122608

CAS No.: 1394808-82-2

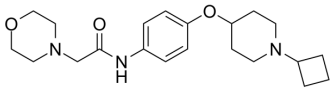
Molecular Formula: $C_{21}H_{31}N_3O_3$

Molecular Weight: 373.49

Target: Histamine Receptor

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

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Samelisant (SUVN-G3031) free base is a potent and selective histamine H3 receptor (H3R) inverse agonist with good brain penetration and oral bioavailability. Samelisant free base 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 free base can be used for the research of sleep-related disorders[1].

In Vitro

Samelisant free base 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 free base 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 free base 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.) free base 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 free base 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 free base 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]. Nirogi R, 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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