GSK1059865

Cat. No.: HY-101534

CAS No.: 1191044-58-2

Molecular Formula: $C_{20}H_{23}BrFN_3O_2$

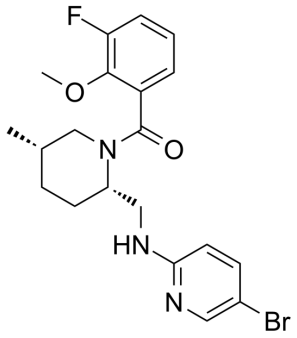
Molecular Weight: 436.32

Target: Orexin Receptor (OX Receptor)

Pathway: GPCR/G Protein; 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 : 200 mg/mL (458.38 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2919 mL	11.4595 mL	22.9190 mL
	5 mM	0.4584 mL	2.2919 mL	4.5838 mL
	10 mM	0.2292 mL	1.1459 mL	2.2919 mL

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

In Vivo

1. Add each solvent one by one: 30% PEG300 >> 70% (10% HP-β-CD in saline)
   Solubility: 5 mg/mL (11.46 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 30 % SBE-β-CD
   Solubility: 3.33 mg/mL (7.63 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

GSK1059865 is a potent orexin 1 receptor antagonist.

IC_{50} & Target

Orexin 1 receptor[1]

In Vivo

Treatment with GSK1059865 significantly decreases ethanol drinking in a dose-dependent manner in CIE-exposed mice. In contrast GSK1059865 decreases drinking in air-exposed mice only at the highest dose used. There is no effect of GSK1059865 on sucrose intake[1]. GSK1059865 (0.3 nM-10 nM) produces non-surmountable antagonism with a dose-dependent rightward shift of the OXA EC_{50} and a concomitant decrease of the agonist maximal response. The calculated pK_B value is 8.77±0.12 for GSK1059865. GSK1059865 (0.1-3.3 μM) produces a classical surmountable profile with parallel rightward shift of the OXA EC_{50} without depression of the agonist maximal response[2]. Intraperitoneal administration of GSK1059865 produces a region-

dependent inhibition of yohimbine-induced relative cerebral blood volume response. The administration of GSK1059865 per se produces a weak relative cerebral blood volume increase in several brain regions. GSK1059865-pretreated animals exhibit slightly higher baseline mean arterial blood pressure values than controls[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1][2]

Rats: GSK1059865 is dissolved in 0.5% HPMC (w/v) in distilled water and administered by gavage at doses of 10 and 30 mg/kg to rats. Drug or vehicle is administered 1 h before access to highly palatable food[2].

Mice: During baseline and the first 5 test cycles following chronic intermittent ethanol (or air) exposure, mice receive vehicle (saline) injections (i.p.; 0.01 ml/g body weight) 30 minutes before drinking ethanol. On test cycles 6 and 7 mice receive vehicle or GSK1059865 (10, 25, 50 mg/kg) before given access to ethanol 15% v/v (Test 6) or sucrose 5% w/v (Test 7) versus water. GSK1059865 is dissolved in saline and TWEEN 80 (0.5 % v/v) as vehicle[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Lopez MF, et al. The highly selective orexin/hypocretin 1 receptor antagonist GSK1059865 potently reduces ethanol drinking in ethanol dependent mice. Brain Res. 2016 Apr 1;1636:74-80.

[2]. Piccoli L, et al. Role of orexin-1 receptor mechanisms on compulsive food consumption in a model of binge eating in female rats. Neuropsychopharmacology. 2012 Aug;37(9):1999-2011.

[3]. Gozzi A, et al. Differential effect of orexin-1 and CRF-1 antagonism on stress circuits: a fMRI study in the rat with the pharmacological stressor Yohimbine. Neuropsychopharmacology. 2013 Oct;38(11):2120-30.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA