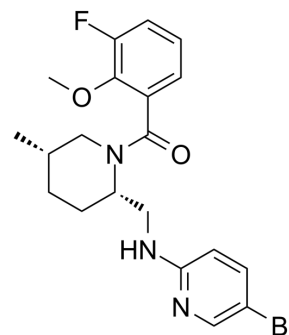


GSK1059865

Cat. No.:	HY-101534	
CAS No.:	1191044-58-2	
Molecular Formula:	C ₂₀ H ₂₃ BrFN ₃ O 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)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	Preparing Stock Solutions	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	<ol style="list-style-type: none"> 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 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.
IC₅₀ & 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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