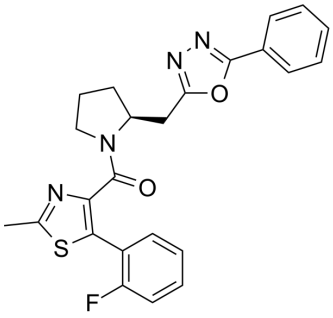
SB-674042

Cat. No.:	HY-10898
CAS No.:	483313-22-0
Molecular Formula:	$C_{24}H_{21}FN_4O_2S$
Molecular Weight:	448.51
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 : 25 mg/mL (55.74 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2296 mL	11.1480 mL	22.2960 mL
	5 mM	0.4459 mL	2.2296 mL	4.4592 mL
	10 mM	0.2230 mL	1.1148 mL	2.2296 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: ≥ 1.43 mg/mL (3.19 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.43 mg/mL (3.19 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.43 mg/mL (3.19 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SB-674042 is a potent and selective non-peptide orexin OX_1 receptor antagonist (K_d=5.03 nM), exhibits 100-fold selectivity for OX_1 over OX_2 receptors with IC_{50} values of 3.76 nM and 531 nM, respectively[1][4].

IC_{50} & Target	OX_1 Receptor	OX_2 Receptor	OX_1 Receptor	OX_2 Receptor
	3.76 nM (IC_{50})	531 nM (IC_{50})	1.1 nM (Ki)	129 nM (Ki)

In Vitro

SB-674042 ([^{3}H]) (0.2-24 nM; 2 h) shows high-affinity and serves as a radio ligand suitable for labelling human OX1 receptors

stably expressed in CHO cells[1].
SB-674042 (5 μM; 4 ⊠ for 30 min, and 37 ⊠ for 3 h) reduces the potency of CB1 receptor agonist (HY-14137) to phosphorylate ERK1/2 in HEK293 cells co-expressing the orexin-1 and CB1 receptors[2].
SB-674042 (1 μM; 24 h) eradicates the increase in mTOR phosphorylation in response to Orexin-A (HY-106224) (1 nM-1 μM; 24 h) in INS-1 cells, indicating activation of the mTOR pathway induced by orexin-A was dependent on the activated OX1 receptor[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[3]

Cell Line:	INS-1 cells
Concentration:	1 μM
Incubation Time:	24 hours; accompanied with 1 μM Orexin-A for 24 hour
Result:	Decreased the phosphorylation level of mTOR induced by Orexin-A.

In Vivo

SB-674042 (0.3 nM/0.3 μL; icv; single dose) reduces contextual and cues fear freezing responses in Stay animals in Stress Alternatives Model (SMA) in mice[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Stress-induced mice model (male C57BL/6NHsd mice, 22-26 g)[4]
Dosage:	0.3 nM/0.3 μL
Administration:	Intracerebroventricular injection; subjected mice to 4 days of social aggression (days 1-4)
Result:	Resulted 39.4% Escape and 60.6% Stay phenotypes among mice.

CUSTOMER VALIDATION

- Neuropharmacology. 17 June 2022, 109168.

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REFERENCES

[1]. Langmead CJ, et al. Characterisation of the binding of [3H]-SB-674042, a novel nonpeptide antagonist, to the human orexin-1 receptor. Br J Pharmacol. 2004 Jan;141(2):340-6.

[2]. Ellis J, et al. Orexin-1 receptor-cannabinoid CB1 receptor heterodimerization results in both ligand-dependent and -independent coordinated alterations of receptor localization and function. J Biol Chem. 2006 Dec 15;281(50):38812-24.

[3]. Chang X, et al. Orexin-A Stimulates Insulin Secretion Through the Activation of the OX1 Receptor and Mammalian Target of Rapamycin in Rat Insulinoma Cells. Pancreas. 2019 Apr;48(4):568-573.

[4]. Yaeger JDW, et al. Orexin 1 Receptor Antagonism in the Basolateral Amygdala Shifts the Balance From Pro- to Antistress Signaling and Behavior. Biol Psychiatry. 2022 May 1;91(9):841-852.

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

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