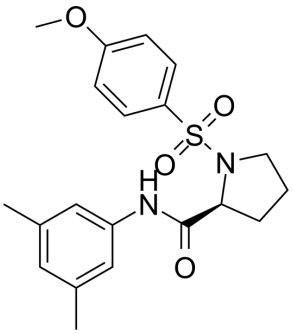
ACT-462206

Cat. No.:	HY-101834
CAS No.:	1361321-96-1
Molecular Formula:	$C_{20}H_{24}N_2O_4S$
Molecular Weight:	388.48
Target:	Orexin Receptor (OX Receptor)
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (257.41 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5741 mL	12.8707 mL	25.7414 mL
5 mM	0.5148 mL	2.5741 mL	5.1483 mL
10 mM	0.2574 mL	1.2871 mL	2.5741 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: ≥ 2.5 mg/mL (6.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.44 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ACT-462206 is an orally active and potent dual Orexin 1/Orexin 2 receptor antagonist with IC_{50}s of 60 nM (Orexin 1) and 11 nM (Orexin 2), respectively. ACT-462206 exhibits brain penetration properties, and can be used for insomnia, stress/anxiety-related disorders and addiction research[1].

IC_{50} & Target	OX2	OX1

In Vitro

Orexins are released in a Ca^{2+}-sensitive manner at axonal terminals and can then bind to two closely related G-protein-coupled receptors (GPCRs): orexin receptor type 1 (OX1) and orexin receptor type 2 (OX2)[1].
ACT-462206 shows binding affinity with K_bs of 17 nM (hOX1), 2.4 nM (hOX2), 28 nM (rOX1), 9.9 nM (rOX2), 27 nM (dOX1), 4.2 nM (dOX2), respectively[1].

ACT-462206 inhibits Orexin activity with IC_{50}s of 60 nM (hOX1), 11 nM (hOX2), 48 nM (rOX1), 9.6 nM (rOX2), 68 nM (dOX1), 26 nM (dOX2), respectively[1].
ACT-462206 inhibits CYP450 3A4T and 3A4M with IC_{50}s of 15 μM and 29 μM, respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

ACT-462206 (compound 24) (100 mg/kg; p.o.; sampling at 3 h) can go cross blood brain barrier, with concentrations are 2267 ng/mL and 1219 ng/g in plasma and brain, respectively in male Wistar rats[1].
ACT-462206 (10-300 mg/kg; p.o.; single dose) shows sleep-promoting effects in male Wistar rats and in male Beagle dogs, with decreasing wakefulness and increasing non-rapid eye movement (non-REM) and REM sleep[1].
ACT-462206 (100, 300 mg/kg; p.o.; single dose) exerts anxiolytic-like effects, decreases the fear-potentiated startle reflexes in response to a sudden loud noise in rats, reduces the socialstress-induced increases of locomotion, body temperature, and heart rate[1].
Pharmacokinetics in different species[1]

	Route	Dose (mg/kg)	AUC (ng•h/mL)	CL (mL/min/kg)	V_{ss} (L/kg)	$t_{1/2}$ (h)	c_{max} (ng/mL)	t_{max} (h)	$F_{1/2}$ (%)
rat	i.v.	1	586	29	1.8	1.9	/	/	/
	p.o.	10	2310	/	/	/	1600	0.5	39
dog	i.v.	1	1490	11	1.4	1.7	/	/	/
	p.o.	3	2750	/	/	/	426	0.5	52

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

Animal Model:	Male Wistar rats[1]
Dosage:	0, 10, 30, 100, 300 mg/kg
Administration:	Oral gavage; single dose
Result:	Decreased the latency to the first persistent episode of non-REM sleep (60 s) and the first persistent episode of REM sleep (30 s). Dose-dependently decreased total wake time and behavioral home cage activity (one-way ANOVA; p <0.001), while increasing REM and non-REM sleep times.

REFERENCES

[1]. Boss C, et al. Structure-activity relationship, biological, and pharmacological characterization of the proline sulfonamide ACT-462206: a potent, brain-penetrant dual orexin 1/orexin 2 receptor antagonist. ChemMedChem. 2014 Nov;9(11):2486-96.

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