Almorexant hydrochloride

Cat. No.: HY-10805A

CAS No.: 913358-93-7

Molecular Formula: $C_{29}H_{32}ClF_3N_2O_3$

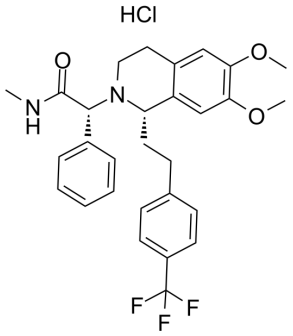
Molecular Weight: 549.02

Target: Orexin Receptor (OX Receptor); Calcium Channel; Caspase; Apoptosis

Pathway: GPCR/G Protein; Neuronal Signaling; Membrane Transporter/Ion Channel; Apoptosis

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 46 mg/mL (83.79 mM)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.8214 mL	9.1071 mL	18.2143 mL
5 mM	0.3643 mL	1.8214 mL	3.6429 mL
10 mM	0.1821 mL	0.9107 mL	1.8214 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 (4.55 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.55 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.55 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Almorexant (ACT 078573) hydrochloride is an orally active, potent and competitive dual orexin receptor antagonist, with K_d values of 1.3 nM (OX1) and 0.17 nM (OX2), respectively. Almorexant hydrochloride reversibly blocks signaling of orexin-A and orexin-B peptides. Almorexant hydrochloride totally blocked the intracellular Ca^{2+} signal pathway. Almorexant hydrochloride stimulates caspase-3 activity in AsPC-1 cells and induces apoptosis[1][2][3][4].

IC_{50} & Target			
	human OX2R 0.17 nM (Kd)	human OX1R 1.3 nM (Kd)	Caspase-3

In Vitro

Almorexant hydrochloride (1 μM) promote tyrosine phosphorylation of SHP2/OX1R complex[1].
Almorexant hydrochloride (1 μM) inhibits the cellular growth of AsPC-1 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Almorexant hydrochloride (1.8 μmol/kg, 100 μL; IP, daily) reduces the volume of tumors[2].
Almorexant hydrochloride (300 mg/kg, PO, once) can help rats to be fully capable of spatial and avoidance learning[4].
Almorexant hydrochloride (30-300 mg/kg) dose-dependently increases rapid eye movement (REM) and non-REM (NREM) sleep and decreases wakefulness apparently without inducing either cataplexy18 or deficits in next-day performance[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mice xenografted with AsPC-1 cells[2]
Dosage:	1.8 μmol/kg, 100 μL
Administration:	IP, daily, starting at day 0 or day 38
Result:	Resulted in a significant decrease in tumor volume when treatment starting at day 0. Started after AsPC-1 tumors were developed (day 38), rapidly and strongly reduced the volume of established tumors.

Animal Model:	Long-Evans rats (24, male, 16-18 weeks of age)[4]
Dosage:	300 mg/kg
Administration:	PO, once
Result:	Successfully learned the spatial task, established spatial memory.

Animal Model:	Male C57BL/6 mice (Orexin/ataxin-3 transgenic (TG) mice and WT mice, 32 ± 0.9 g, age 15 ± 0.5 week)[3]
Dosage:	30, 100, 300 mg/kg (3, 10, and 30 mg/mL; 10 mL/kg)
Administration:	IP, once every 3 days
Result:	Exacerbated cataplexy in TG mice and increased nonrapid eye movement (NREM) sleep with heightened sleep/wake fragmentation in both genotypes during the 12-h dark period after dosing. Showed greater hypnotic potency in WT mice than in TG mice.

CUSTOMER VALIDATION

- Cell Metab. 2018 Jul 3;28(1):118-129.e5.
- bioRxiv. 2023 Jul 19.
- Oncotarget. 2018 Jan 9;9(6):6952-6967.

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REFERENCES

[1]. Dayot S, et al. In vitro, in vivo and ex vivo demonstration of the antitumoral role of hypocretin-1/orexin-A and almorexant in pancreatic ductal adenocarcinoma.

Oncotarget. 2018 Jan 9;9(6):6952-6967.

[2]. Malherbe P, et al. Biochemical and electrophysiological characterization of almorexant, a dual orexin 1 receptor (OX1)/orexin 2 receptor (OX2) antagonist: comparison with selective OX1 and OX2 antagonists. Mol Pharmacol. 2009 Sep;76(3):618-31.

[3]. Black SW, et al. Almorexant promotes sleep and exacerbates cataplexy in a murine model of narcolepsy. Sleep. 2013 Mar 1;36(3):325-36.

[4]. Dietrich H, et al. Intact learning and memory in rats following treatment with the dual orexin receptor antagonist almorexant. Psychopharmacology (Berl). 2010 Oct;212(2):145-54.

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