Almorexant

Cat. No.: HY-10805

CAS No.: 871224-64-5

Molecular Formula: $C_{29}H_{31}F_3N_2O_3$

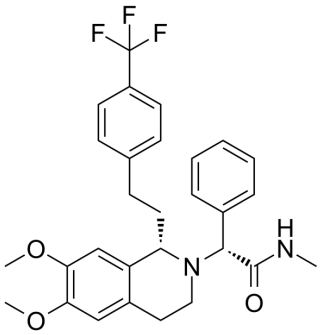
Molecular Weight: 512.56

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

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

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 : ≥ 46 mg/mL (89.75 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9510 mL	9.7550 mL	19.5099 mL
5 mM	0.3902 mL	1.9510 mL	3.9020 mL
10 mM	0.1951 mL	0.9755 mL	1.9510 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 (4.88 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.88 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.88 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Almorexant (ACT 078573) 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 reversibly blocks signaling of orexin-A and orexin-B peptides. Almorexant totally blocked the intracellular Ca^{2+} signal pathway. Almorexant stimulates caspase-3 activity in AsPC-1 cells and induces apoptosis[1][2][3][4].

IC_{50} & Target	human OX2R	human OX1R	Caspase-3

	0.17 nM (Kd)	1.3 nM (Kd)	

In Vitro

Almorexant (1 μM) promotes tyrosine phosphorylation of SHP2/OX1R complex[1].
Almorexant (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 (1.8 μmol/kg, 100 μL; IP, daily) reduces the volume of tumors[2].
Almorexant (300 mg/kg, PO, once) can help rats to be fully capable of spatial and avoidance learning[4].
Almorexant (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]. 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.

[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]. 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.

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