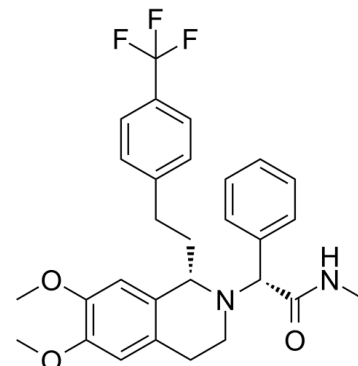


Data Sheet

Product Name:	Almorexant
Cat. No.:	CS-2484
CAS No.:	871224-64-5
Molecular Formula:	C ₂₉ H ₃₁ F ₃ N ₂ O ₃
Molecular Weight:	512.56
Target:	Apoptosis; Calcium Channel; Caspase; Orexin Receptor (OX Receptor)
Pathway:	Apoptosis; GPCR/G Protein; Membrane Transporter/Ion Channel; Neuronal Signaling
Solubility:	DMSO : ≥ 46 mg/mL (89.75 mM)



BIOLOGICAL ACTIVITY:

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 **Ca²⁺** signal pathway. Almorexant stimulates **caspase-3** activity in AsPC-1 cells and induces **apoptosis**^{[1][2][3][4]}. IC₅₀ & Target: K_d: 0.17 nM (hOX2), 1.3 nM (hOX1)^[2] **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]. **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 cataplexy or deficits in next-day performance^[3].

PROTOCOL (Extracted from published papers and Only for reference)

Animal administration [3] In a two-way mixed (between-within) design, orexin/ataxin-3 transgenic(TG) and wild type (WT) mice are dosed intraperitoneally with Almorexant (30, 100, and 300 mg/kg), QNP (0.5 mg/kg) as a positive control for cataplexy, or VEH. Treatments are administered in a counterbalanced crossover design once every 3 days. Dosing occurred at the beginning of the dark/active phase at Zeitgeber Time (ZT) 12. Physiologic data and video-recorded behavioral data are collected over the following 12 h when the propensity for cataplexy is greatest and hypnotic effects are most evident in nocturnal species.

References:

- [1]. 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.
- [2]. Black SW, et al. Almorexant promotes sleep and exacerbates cataplexy in a murine model of narcolepsy. *Sleep*. 2013 Mar 1;36(3):325-36.
- [3]. 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.
- [4]. Dietrich H, et al. Intact learning and memory in rats following treatment with the dual orexin receptor antagonist almorexant. *Psychopharmacology (Berl)*.

CAIndexNames:

2(1H)-Isoquinolineacetamide, 3,4-dihydro-6,7-dimethoxy-N-methyl- α -phenyl-1-[2-[4-(trifluoromethyl)phenyl]ethyl]-, (α R,1S)-

SMILES:

CNC([C@@H](C1=CC=CC=C1)N2CCC3=CC(OC)=C(OC)C=C3[C@@H]2CCC4=CC=C(C(F)(F)F)C=C4)=O

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

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