JTC-801

Cat. No.: HY-13274

CAS No.: 244218-51-7

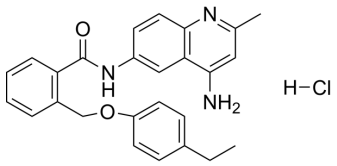
Molecular Formula: $C_{26}H_{26}ClN_3O_2$

Molecular Weight: 447.96

Target: Opioid Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

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 : 100 mg/mL (223.23 mM; Need ultrasonic)
H_2O : ≥ 0.33 mg/mL (0.74 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2323 mL	11.1617 mL	22.3234 mL
5 mM	0.4465 mL	2.2323 mL	4.4647 mL
10 mM	0.2232 mL	1.1162 mL	2.2323 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 (5.58 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.58 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.58 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JTC-801 is a selective opioid receptor-like1 (ORL1) receptor antagonist, binding to ORL1 receptor with a K_i value of 8.2 nM.

IC_{50} & Target

NOP Receptor/ORL1

In Vitro

JTC-801 inhibits [^{3}H]-nociceptin binding to ORL1 receptor expressed in HeLa cells with an IC_{50} value of 94±8.6 nm at a [^{3}H]-nociceptin concentration of 50?pM. JTC-801 weakly inhibits the binding of the ligands to human δ receptor (IC_{50}>10?μM), κ receptor (IC_{50}>10?μM), and μ receptor (IC_{50}=325?nM). In rat cerebrocortical membrane, JTC-801 inhibits ORL1 receptor (IC_{50}

	=472?nM) and μ receptor (IC_{50}=1831?nM). JTC-801 at a concentration of 10?μM reverses the inhibitory action of nociceptin against forskolin-induced increase in cyclic AMP level (IC_{50}: 2.58?μM, 1?nM of nociceptin used). JTC-801 alone does not affect the the production of cyclic AMP[1]. The affinity of JTC-801 for ORL1 receptor, human opioid μ-, κ-, and δ-receptors is 8.2 nM, 102.9 nM, 1057.5 nM and 8647.2 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	JTC-801 (≥0.01?mg/kg, i.v. or 1?mg/kg, p.o.) antagonizes the nociceptin-induced allodynia in mice. In mouse hot-plate test, JTC-801 prolongs escape response latency (ERL) to exposed heat stimulus with minimum effective doses (MED) of 0.01?mg/kg by i.v. or 1?mg/kg by p.o. In the rat formalin test, JTC-801 reduces both the first and second phases of the nociceptive response with MED of 0.01?mg/kg by i.v. administration or 1?mg/kg by p.o. administration. This anti-nociceptive action of JTC-801 is not inhibited by naloxone (10?mg/kg, s.c.). JTC-801 antagonizes the ORL1 receptor response, and has efficacious and potent anti-nociceptive effects in acute pain animal models not only by intravenous injection but also oral administration[1]. JTC-801 (0.3 mg/kg) decreases allodynia induced by the intrathecal injection of nociceptin in mice[2]. JTC-801 (6 mg/kg i.p., once daily) reverses SPS-induced mechanical allodynia, thermal hyperalgesia, anxiety-like behaviour and hypocortisolism. JTC-801 treatment also reverses NOP receptor protein and mRNA up-regulation in amygdala and PAG. JTC-801 blocks elevated N/OFQ levels in serum, CSF, PAG and hippocampus at day 21 of SPS[3]. JTC-801 (0.05-5 mg/kg, i.p.) supresses the the analgesic effect of N2O in 129Sv mice by the writhing test and tail flick test[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	A suspension of membranes from human μ-opioid receptor-expressing CHO-K1 cells in 50 mM Tris-HCl buffer (pH 7.4) containing 5 mM $MgCl_2$ and 10% sucrose is incubated at room temperature for 2.5 h with 0.33 nM ^{3}H-labeled diprenorphine and various concentrations of JTC-801. The membranes are collected by filtration using Whatman 934-AH, and radioactivity is counted with a TopCount A9912V scintillation counter. Nonspecific binding (6.4%) is determined with 10 μM naloxone. Specific binding is calculated by subtracting nonspecific binding from the total binding. Data are the mean±SE (n=3). MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	The antagonistic effect of naloxone, a non-specific opioid antagonist, on the anti-nociceptive effect of JTC-801 and morphine is examined by formalin stimulation test. Limb licking response is induced by subcutaneous injection of 50 μL of 5% formalin to the left hind limb of each rat. The first 5 min (from immediately after the injection of formalin) and the subsequent 15 min (15-30 min post-injection) are designated as the first and second phases, respectively. The limb licking time during each of the phases is measured and used as an indicator of pain. Fifteen min before the injection of formalin, naloxone (10 mg/kg, dissolved in physiological saline) is given subcutaneously. Five min before the injection of formalin, JTC-801 and morphine are dissolved in 5% sorbitol and given into the tail vein at doses of 0.03 and 1.0 mg/kg, respectively. JTC-801 (3.0 mg/kg) and morphine (30 mg/kg) are administered orally 60 min before the formalin injection. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Oncol Lett. 2019 Feb;17(2):1939-1945.
- J Recept Signal Transduct Res. 2018 Apr;38(2):133-140.
- Pharmazie. 2018 May 1;73(5):283-287.
- Med Sci (Paris). 2018 Oct;34 Focus issue F1:8-14.

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REFERENCES

[1]. Yamada H, et al. Pharmacological profiles of a novel opioid receptor-like1 (ORL(1)) receptor antagonist, JTC-801. Br J Pharmacol, 2002, 135(2), 323-332.

[2]. Shinkai H, et al. 4-Aminoquinolines: novel nociceptin antagonists with analgesic activity. J Med Chem, 2000, 43(24), 4667-4677.

[3]. Zhang Y, et al. Nociceptin/orphanin FQ peptide receptor antagonist JTC-801 reverses pain and anxiety symptoms in a rat model of post-traumatic stress disorder. Br J Pharmacol. 2015 Jan;172(2):571-82.

[4]. Koyama T, et al. Nociceptin receptor antagonist JTC-801 inhibits nitrous oxide-induced analgesia in mice. J Anesth. 2009;23(2):301-3.

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