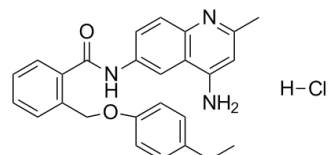


Data Sheet

Product Name:	JTC-801
Cat. No.:	HY-13274
CAS No.:	244218-51-7
Molecular Formula:	C ₂₆ H ₂₆ ClN ₃ O ₂
Molecular Weight:	447.96
Target:	Opioid Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Solubility:	10 mM in DMSO



BIOLOGICAL ACTIVITY:

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

IC₅₀ & Target: K_i: 8.2 nM (ORL1)^[2]

In Vitro: JTC-801 inhibits [³H]-nociceptin binding to ORL1 receptor expressed in HeLa cells with an IC₅₀ value of 94±8.6 nM at a [³H]-nociceptin concentration of 50 pM. JTC-801 weakly inhibits the binding of the ligands to human δ receptor (IC₅₀>10 μM), κ receptor (IC₅₀>10 μM), and μ receptor (IC₅₀=325 nM). In rat cerebrocortical membrane, JTC-801 inhibits ORL1 receptor (IC₅₀=472 nM) and μ receptor (IC₅₀=1831 nM). JTC-801 at a concentration of 10 μM reverses the inhibitory action of nociceptin against forskolin-induced increase in cyclic AMP level (IC₅₀: 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].

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.) suppresses the the analgesic effect of N2O in 129Sv mice by the writhing test and tail flick test^[4].

PROTOCOL (Extracted from published papers and Only for reference)

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 MgCl₂ and 10% sucrose is incubated at room temperature for 2.5 h with 0.33 nM ³H-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).

Animal Administration: JTC-801 is dissolved in 5% sorbitol.^[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.

References:

- [1]. Yamada H, et al. Pharmacological profiles of a novel opioid receptor-like1 (ORL1) 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.

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

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