

Product Data Sheet

Product Name: JDTic 2HCl

Cat. No.: GC17624

Chemical Properties

Cas. No. 785835-79-2

Chemical Name (3R)-7-hydroxy-N-[(2S)-1-[(3R,4R)-4-(3-hydroxyphenyl)-3,4-dimethylpiperidin-1-yl]-3-methylbutan-2-yl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide dihydrochloride

SMILES CC1CN(CCC1(C)C2=CC(=CC=C2)O)CC(C(C)C)NC(=O)C3CC4=C(CN3)C=C(C=C4)O.Cl.Cl

Formula C₂₈H₄₁Cl₂N₃O₃ M.Wt 538.55

Solubility DMSO : 100 mg/mL (185.68 mM; Need ultrasonic); H₂O : 50 mg/mL (92.84 mM; Need ultrasonic) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

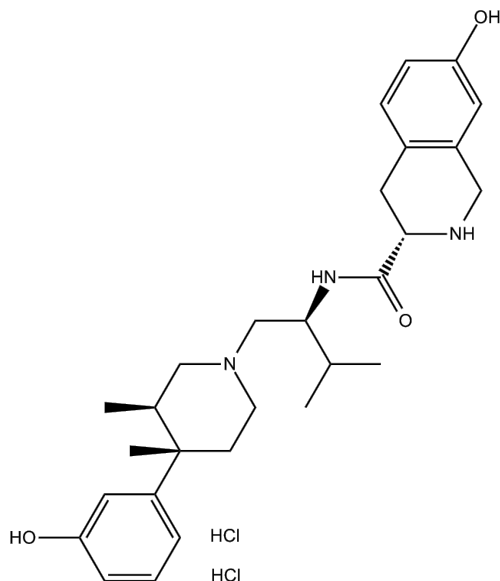
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment: [1]

Cell lines HEK293 cells expressing KOPr-GFP

Preparation method The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

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Reaction Conditions 10 μ M, 60 min

Applications The compound was administered for 60 min before lysing the cells. And pJNK-ir intensities were examined by Western blot analysis. JDtic significantly increased phospho-JNK-ir at 10 μ M.

Animal experiment: [2]

Animal models Male Wistar rats

Dosage form Intraperitoneal injection, 3, or 10 mg/kg at 1 ml/kg, dissolved in sterile water

Applications Post-hoc analysis using Newman-Keuls test indicated a significant difference from baseline responding only in the JDtic 10 mg/kg pretreated group at the 2 h pretreatment time point ($p=0.002$). Furthermore, there was also a significant decrease observed in the 10 mg/kg JDtic treated group when compared to vehicle control at the 2 h time point, while the groups were virtually identical at later time points.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1] Melief E J, Miyatake M, Carroll F I, et al. Duration of action of a broad range of selective κ -opioid receptor antagonists is positively correlated with c-Jun N-terminal kinase-1 activation. *Molecular pharmacology*, 2011, 80(5): 920-929.

[2] Schank J R, Goldstein A L, Rowe K E, et al. The kappa opioid receptor antagonist JD_{Tic} attenuates alcohol seeking and withdrawal anxiety. *Addiction biology*, 2012, 17(3): 634-647.

Background

JD_{Tic} is a selective inhibitor of kappa opioid receptor with IC₅₀ value of 0.02nM [1].

JD_{Tic} is one of the kappa opioid receptor selective antagonists. These antagonists are thought as potential pharmacotherapies for addiction, anxiety disorders, depression, psychosis disorders and obesity. Because of the unique structural feature of JD_{Tic}, it is more selective and potent for KOR activity than other KOR antagonists. JD_{Tic} is shown to block the antinociceptive response of nicotine in the tail-flick test with a dose-dependent manner. It (8 mg/kg) can also block the nicotine withdrawal signs in mice via effecting the expression of a CPA associated with nicotine withdrawal. Additionally, JD_{Tic} is also reported to decrease the number of somatic withdrawal signs in morphine-dependent rats [2,3].

References:

[1] Michael P. Hedrick, Palak Gosalia, Kelin Li, Kevin Frankowski, Shenghua Shi, Thomas E. Prisinzano, Frank Schoenen, Jeffrey Aubé, Ying Su, S. Vasile, Eduard Sergienko, Wilson Gray, Santosh Hariharan, Loribelle Milan, Susanne Heynen-Genel, Bryan L. Roth, Jon Evans, Vincent Setola, Thomas D.Y. Chung, Marc Caron, Laura M. Bohn and Lawrence S. Barak. Antagonist for the Kappa Opioid Receptor. *Molecular Libraries*. 2011 Jun: 1-32.

[2] Scott P. Runyon, Lawrence E. Brieady, S. Wayne Mascarella, James B. Thomas, Hernán A. Navarro, James L. Howard, Gerald T. Pollard, and F. Ivy Carroll. Analogues of (3R)-7-Hydroxy-N-[(1S)-1-[[[(3R,4R)-4-(3-hydroxyphenyl)-3,4-dimethyl-1-piperidinyl]methyl]-2-methylpropyl]-1,2,3,4-tetrahydro-3-isoquinolinecarboxamide(JD_{Tic}). *Synthesis and In Vitro and In Vivo Opioid Receptor Antagonist Activity*. *J Med Chem*. 2010 July, 53(14): 5290–5301.

[3] K. J. Jackson, Frank Ivy Carroll, S. S. Negus and M. I. Damaj. Effect of the selective kappa-opioid receptor antagonist JD_{Tic} on nicotine antinociception, reward, and withdrawal in the mouse.

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Psychopharmacology (Berl). 2010 June, 210(2): 285–294.

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