

Product Data Sheet

Product Name: ZD 7288
Cat. No.: GC10578

Chemical Properties

Cas. No. 133059-99-1

Chemical Name (E)-N-ethyl-1,2-dimethyl-6-(methylimino)-N-phenyl-1,6-dihydropyrimidin-4-amine hydrochloride

SMILES CCN(C1=CC=CC=C1)C2=C/C(N(C)C(C)=N2)=N/C.Cl

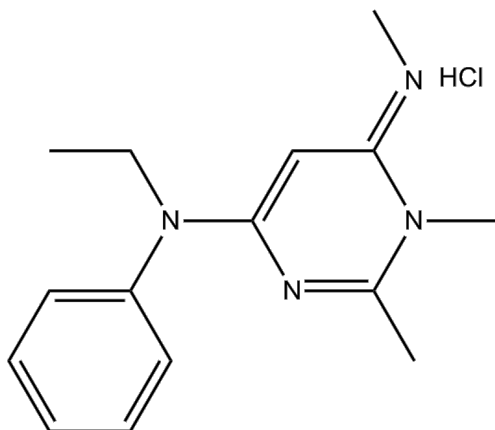
Formula $C_{15}H_{21}ClN_4$ M.Wt 292.81

Solubility 50mg/mL in ethanol, 30mg/mL in DMSO or DMF; Water : ≥ 50 mg/mL (170.76 mM) Storage Store at 2-8°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.

Structure



Protocol

Cell experiment [1]:

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

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Cell lines Mouse embryonic stem cells (mESCs)

Preparation Method Cell proliferation was determined in 24-well plates by simple cell counting techniques. mESCs were treated with different concentrations of ZD 7288 for the entire period of the experiments. Medium was changed daily. Cells were collected at different time points for cell counting. Cells treated with equal volume of water (solvent for ZD 7288) were used as control. Numbers of viable and nonviable cells were determined by trypan blue exclusion assay.

Reaction
Conditions 0.1-30 μ M; 72h

Applications ZD 7288 decreased the proportion of cells in G0/G1 phase and increase the proportion of cells in S phase.

Animal experiment [2]:

Animal models Shrews

Preparation Method Daily food restriction was initiated 2 hours before the start of the experiment, but before the injection of the emetic, each shrew was given 3-4 mealworms to aid in the identification of wet vomit, as previously reported. For systemic dose-response emesis studies, groups of shrews were injected with different doses of ZD 7288 (0, 0.05, 0.25, and 1 mg/kg, intraperitoneally, n = 8 shrews per group).

Dosage form 0-1 mg/kg; ip; single injection

Applications ZD 7288 induces vomiting in a dose-dependent manner.

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References:

- [1]. Lau Y T, Wong C K, Luo J, et al. Effects of hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers on the proliferation and cell cycle progression of embryonic stem cells[J]. Pflügers Archiv-European Journal of Physiology, 2011, 461(1): 191-202.
- [2]. Zhong W, Darmani N A. The Hcn Channel blocker Zd7288 induces Emesis in the least shrew (Cryptotis parva)[J]. Frontiers in Pharmacology, 2021, 12: 647021.

Background

ZD 7288 is a hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker [1]. ZD 7288 reduces cellular spontaneous activity and excitability by reducing If/Ih currents [2]. ZD 7288 is commonly used in areas such as arrhythmias, neuropathic pain, or irritable bowel syndrome (IBS) [3-4].

In mouse embryonic stem cells, ZD 7288 (0.1-30 μ M; 72h) decreased the proportion of cells in G0/G1 phase and increase the proportion of cells in S phase [5]. In HEK293 cells, ZD 7288 (0.1-100 μ M; 2h) inhibits Na⁺ currents in cells transfected with Na_v 1.4 plasmid [6]. In α -TC6 cells, blocking HCN channels with ZD 7288 (100 μ M; 30min) significantly increases the intracellular calcium concentration [7].

In shrews, ZD 7288 (0-1mg/kg; ip; single injection) induces vomiting in a dose-dependent manner [8]. In C57BL/6 mice, ZD 7288 (6.25 μ g/kg, 12.5 μ g/kg; ip; single injection) inhibits sevoflurane-induced agitation [9].

References:

- [1]. Zhang X, Min X, Xu X, et al. ZD7288, a selective hyperpolarization-activated cyclic nucleotide-gated channel blocker, inhibits hippocampal synaptic plasticity[J]. Neural Regeneration Research, 2016, 11(5): 779-786.
- [2]. Gasparini S, DiFrancesco D. Action of the hyperpolarization-activated current (I_h) blocker ZD 7288 in hippocampal CA1 neurons[J]. Pflügers Archiv, 1997, 435(1): 99-106.
- [3]. Chen Y, Lin C, Tang Y, et al. ZD 7288, an HCN channel blocker, attenuates chronic visceral pain in irritable bowel syndrome-like rats[J]. World journal of gastroenterology: WJG, 2014, 20(8): 2091.

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- [4]. Yang L, Liu X, Yao K, et al. HCN channel antagonist ZD7288 ameliorates neuropathic pain and associated depression[J]. Brain Research, 2019, 1717: 204-213.
- [5]. Lau Y T, Wong C K, Luo J, et al. Effects of hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers on the proliferation and cell cycle progression of embryonic stem cells[J]. Pflügers Archiv-European Journal of Physiology, 2011, 461(1): 191-202.
- [6]. Wu X, Liao L, Liu X, et al. Is ZD7288 a selective blocker of hyperpolarization-activated cyclic nucleotide-gated channel currents?[J]. Channels, 2012, 6(6): 438-442.
- [7]. Zhang Y, Zhang N, Gyulkhandanyan A V, et al. Presence of functional hyperpolarisation-activated cyclic nucleotide-gated channels in clonal alpha cell lines and rat islet alpha cells[J]. Diabetologia, 2008, 51(12): 2290-2298.
- [8]. Zhong W, Darmani N A. The Hcn Channel blocker Zd7288 induces Emesis in the least shrew (Cryptotis parva)[J]. Frontiers in Pharmacology, 2021, 12: 647021.
- [9]. Liang P, Xu-Bin H, Feng-Shan L, et al. Hyperpolarization-Activated Cyclic Nucleotide-Gated Channel Blocker ZD7288 Prevents Sevoflurane-Induced Hyperactivity in A Novel Mice Behavioral Model[J]. Journal of Anesthesia and Perioperative Medicine (JAPM), 2017, 4(5): 205.

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