

Product Data Sheet

Product Name: Danegaptide Hydrochloride

Cat. No.: GC35807

Chemical Properties

Cas. No. 943133-81-1

SMILES O=C(N[C@H]1CN(C(CN)=O)[C@H](C(O)=O)C1)C2=CC=CC=C2.[H]Cl

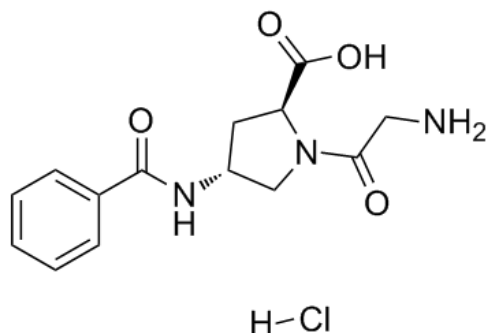
Formula $C_{14}H_{18}ClN_3O_4$ M.Wt 327.76

Solubility Water: ≥ 75 mg/mL (228.83 mM); Storage Store at -20°C
DMSO: ≥ 55 mg/mL (167.81 mM)

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



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

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Protocol

Cell experiment [1]:

Cell lines Rat Retinal Endothelial Cells (RRECs)

Preparation Method RRECs were maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum (FBS), antimycotics, and antibiotics at 37°C, 5% CO₂. Cells were grown in high glucose (HG; 30mM) medium for 3, 5, or 7 days until confluence. Cells grown in HG medium were exposed to Danegaptide Hydrochloride (100nM).

Reaction
Conditions 100nM; 3, 5, and 7 days.

Applications Danegaptide Hydrochloride significantly preserved gap junction intercellular communication (GJIC) activity in RRECs under high glucose condition. Danegaptide Hydrochloride significantly prevented high glucose-induced apoptosis, also significantly reduced high glucose-induced excess cell monolayer permeability.

Animal experiment [2]:

Animal models Sprague-Dawley rats

Preparation Method Rats were subjected to focal cerebral ischemia via middle cerebral artery occlusion (MCAO). Danegaptide Hydrochloride was dissolved in distilled water and administered intraperitoneally at a dose of 3mg/kg twice daily, starting from day 3 post-ischemia until sacrifice.

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Dosage form 3mg/kg; i.p.

Applications

Danegaptide Hydrochloride administration significantly improved neurological behavior scores in balance beam walking and Y-maze tests, increased dendritic spine density in hippocampal CA1 and DG regions, alleviated synaptic ultrastructure destruction, and upregulated the expression of synaptic plasticity markers synaptophysin (SYN) and growth-associated protein-43 (GAP-43) compared to the MCAO group.

References:

- [1] Kim D, Mouritzen U, Larsen BD, et al. Inhibition of Cx43 gap junction uncoupling prevents high glucose-induced apoptosis and reduces excess cell monolayer permeability in retinal vascular endothelial cells. *Exp Eye Res.* 2018 Aug;173:85-90.
- [2] Yang K, Zhou Y, Zhou L, et al. Synaptic Plasticity After Focal Cerebral Ischemia Was Attenuated by Gap26 but Enhanced by GAP-134. *Front Neurol.* 2020 Aug 26;11:888.

Background

Danegaptide Hydrochloride is a potent, selective, and orally active gap-junction modifier^[1]. Danegaptide Hydrochloride optimizes intercellular communication in cardiac cells by regulating electrical signal transduction, thereby restoring or improving normal heart rhythm^[2]. Danegaptide Hydrochloride can reduce the occurrence of arrhythmic events such as atrial fibrillation^[3]. Danegaptide Hydrochloride can protect the heart from harmful stimuli like ischemia/reperfusion injury^[4].

In vitro, pretreatment of human proximal tubule epithelial cells (hPTECs) with Danegaptide Hydrochloride (50–100nM) for 48 hours, followed by stimulation with TGFβ1 (10ng/ml), significantly blocked connexin 43 (Cx43)-mediated hemichannel activity and inhibited ATP release^[5]. Pretreatment of rat retinal vascular endothelial cells (RRECs) with Danegaptide Hydrochloride (100nM) for 3–7 days, followed by high glucose (30mM) stimulation, significantly maintained gap

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junction intercellular communication (GJIC) activity^[6].

In vivo, intraperitoneal administration of Danegaptide Hydrochloride (3mg/kg twice daily) starting from day 3 after middle cerebral artery occlusion (MCAO) and continuing for two weeks in MCAO rats significantly improved neurological behavior, increased dendritic spine density in the hippocampal CA1 and DG regions, alleviated synaptic ultrastructural damage, and upregulated the expression of synaptic plasticity markers SYN and GAP-43, promoting synaptic plasticity and neurological functional recovery after focal cerebral ischemia^[7]. Oral administration of Danegaptide Hydrochloride (5mg/kg/day) via drinking water to Scn5a^{+/-} mice from 45 weeks of age until 60 weeks significantly increased the expression and Ser368 phosphorylation of cardiac connexin 43 (Cx43), prevented Cx43 mislocalization, suppressed the development of ventricular fibrosis, and reduced abnormal proliferation of cardiac fibroblasts, thereby inhibiting age-dependent myocardial fibrosis progression^[8].

References:

- [1] Dhein S, Hagen A, Jozwiak J, et al. Improving cardiac gap junction communication as a new antiarrhythmic mechanism: the action of antiarrhythmic peptides. *Naunyn Schmiedeberg's Arch Pharmacol*. 2010 Mar;381(3):221-34.
- [2] Piatnitski Chekler EL, Butera JA, et al. Discovery of a class of potent gap-junction modifiers as novel antiarrhythmic agents. *Bioorg Med Chem Lett*. 2009 Aug 15;19(16):4551-4.
- [3] Rossman EI, Liu K, Morgan GA, et al. The gap junction modifier, GAP-134 [(2S,4R)-1-(2-aminoacetyl)-4-benzamido-pyrrolidine-2-carboxylic acid], improves conduction and reduces atrial fibrillation/flutter in the canine sterile pericarditis model. *J Pharmacol Exp Ther*. 2009 Jun;329(3):1127-33.
- [4] Hennen JK, Swillo RE, Morgan GA, et al. GAP-134 [(2S,4R)-1-[2-aminoacetyl]4-benzamidopyrrolidine-2-carboxylic acid) prevents spontaneous ventricular arrhythmias and reduces infarct size during myocardial ischemia/reperfusion injury in open-chest dogs. *J Cardiovasc Pharmacol Ther*. 2009 Sep;14(3):207-14.
- [5] Squires PE, Price GW, Mouritzen U, et al. Danegaptide Prevents TGFβ1-Induced Damage in Human Proximal Tubule Epithelial Cells of the Kidney. *Int J Mol Sci*. 2021 Mar 10;22(6):2809.
- [6] Kim D, Mouritzen U, Larsen BD, et al. Inhibition of Cx43 gap junction uncoupling prevents high glucose-induced apoptosis and reduces excess cell monolayer permeability in retinal vascular endothelial cells. *Exp Eye Res*. 2018 Aug;173:85-90.
- [7] Yang K, Zhou Y, Zhou L, et al. Synaptic Plasticity After Focal Cerebral Ischemia Was Attenuated

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by Gap26 but Enhanced by GAP-134. Front Neurol. 2020 Aug 26;11:888.

[8] Patin J, Castro C, Steenman M, et al. Gap-134, a Connexin43 activator, prevents age-related development of ventricular fibrosis in Scn5a^{+/-} mice. Pharmacol Res. 2020 Sep;159:104922.

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