

Product Data Sheet

Product Name: NPS-2143

Cat. No.: GC16943

Chemical Properties

Cas. No. 284035-33-2

Chemical Name 2-chloro-6-[(2R)-2-hydroxy-3-[(2-methyl-1-naphthalen-2-yl)propan-2-yl)amino]propoxy]benzonitrile

SMILES CC(C)(CC1=CC2=CC=CC=C2C=C1)NCC(COC3=C(C(=CC=C3)Cl)C#N)O

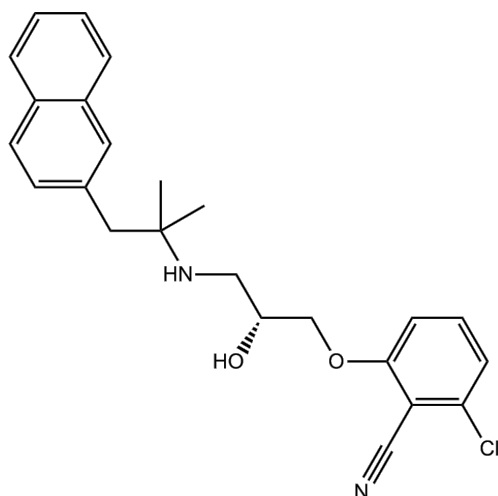
Formula C₂₄H₂₅ClN₂O₂ M.Wt 408.93

Solubility ≥ 40.9mg/mL in DMSO 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.

Structure



Protocol

Cell experiment [1]:

Cell lines Breast cancer cell lines MDA-MB-231 and MCF-7

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

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Preparation Method The biological effects of various concentrations of NPS-2143 on breast cancer cell proliferation were measured by in vitro MTT assay.

Reaction Conditions 0.5-10 μ M; 48h

Applications The cell viability of both MDA-MB-231 and MCF-7 cells was reduced after NPS-2143 treatment in a dose-dependent manner.

Animal experiment [2]:

Animal models Wild-type, Nuf/+, and Nuf/Nuf mice

Preparation Method A single bolus of NPS-2143 or vehicle (15% aqueous solution of 2-hydroxypropyl- β -cyclodextrin) was administered to mice. Plasma samples were obtained at either 0, 1, 4, or 24 hours by tail vein or terminal bleed.

Dosage form 30mg/kg; once; i.p.

Applications NPS-2143 successfully improved the hypocalcemia associated with Nuf/+ and Nuf/Nuf mice compared with mice given the drug vehicle alone or untreated mice. At 4 hours after NPS 2143 administration, plasma calcium values remained significantly elevated in wild-type and affected Nuf/+ mice compared with respective untreated mice.

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References:

[1]. Alqudah MAY, Azaizeh M, et al. Calcium-Sensing Receptor Antagonist NPS-2143 Inhibits Breast Cancer cell Proliferation, Migration and Invasion via Downregulation of p-ERK1/2, Bcl-2 and Integrin β 1 and Induces Caspase 3/7 Activation. Adv Pharm Bull. 2022 Mar;12(2):383-388.

[2]. Hannan FM, Walls GV, et al. The Calcilytic Agent NPS 2143 Rectifies Hypocalcemia in a Mouse Model With an Activating Calcium-Sensing Receptor (CaSR) Mutation: Relevance to Autosomal Dominant Hypocalcemia Type 1 (ADH1). Endocrinology. 2015 Sep;156(9):3114-21.

Background

NPS-2143 is an orally active calcium-sensing receptor (CaSR) antagonist that induces an increase in cytosolic Ca^{2+} concentration, with an IC_{50} of 43nM. NPS-2143 stimulates the release of parathyroid hormone^[1].

NPS-2143 (100nM; 30min) effectively inhibits the secretion of cytokines and chemokines induced by $\text{fA}\beta_{25-35}$ in NHA cell, including IL-6, MCP-2, RANTES, and s-ICAM-1 ^[2]. NPS-2143 significantly inhibits cell proliferation in MDA-MB-231 and MCF-7 cells, with IC_{50} values of 4.08 μ M and 5.71 μ M, respectively. In MDA-MB-231 cells, NPS-2143 induces caspase-3/7 activation while significantly reducing the expression of the anti-apoptotic protein Bcl-2. Additionally, NPS-2143 inhibits the migration and invasion of MDA-MB-231 cells and significantly downregulates the expression of p-ERK1/2 and integrin β 1 proteins^[3].

NPS-2143 (30mg/kg) was administered as a single intraperitoneal injection to wild-type and Nuf mice, plasma calcium and PTH concentrations, as well as urinary calcium excretion were measured. NPS-2143 caused a significant increase in plasma calcium and PTH levels in Nuf mice but did not increase urinary calcium excretion. NPS-2143 normalized the gain-of-function mutation causing ADH1 and ameliorated the hypocalcemia associated with the disease^[4].

References:

[1].Wang S, Qiu L, et al. NPS - 2143 (hydrochloride) inhibits melanoma cancer cell proliferation and induces autophagy and apoptosis. Med Sci (Paris). 2018 Oct;34 Focus issue F1:87-93.

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[2].Chiarini A, Armato U, et al. CaSR Antagonist (Calcilytic) NPS 2143 Hinders the Release of Neuroinflammatory IL-6, Soluble ICAM-1, RANTES, and MCP-2 from A β -Exposed Human Cortical Astrocytes. Cells. 2020 Jun 2;9(6):1386.

[3].Alqudah MAY, Azaizeh M, et al. Calcium-Sensing Receptor Antagonist NPS-2143 Inhibits Breast Cancer cell Proliferation, Migration and Invasion via Downregulation of p-ERK1/2, Bcl-2 and Integrin β 1 and Induces Caspase 3/7 Activation. Adv Pharm Bull. 2022 Mar;12(2):383-388.

[4].Hannan FM, Walls GV, et al. The Calcilytic Agent NPS 2143 Rectifies Hypocalcemia in a Mouse Model With an Activating Calcium-Sensing Receptor (CaSR) Mutation: Relevance to Autosomal Dominant Hypocalcemia Type 1 (ADH1). Endocrinology. 2015 Sep;156(9):3114-21.

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