

Product Data Sheet

Product Name: Fingolimod (FTY720) HCl

Cat. No.: GC14807

Chemical Properties

Cas. No. 162359-56-0

Chemical Name 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol;hydrochloride

SMILES CCCCCCCCC1=CC=C(C=C1)CCC(CO)(CO)N.Cl

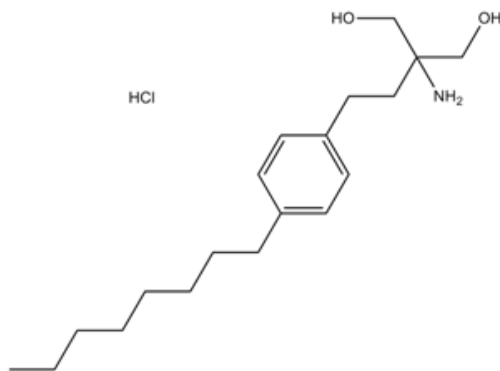
Formula $C_{19}H_{34}ClNO_2$ M.Wt 343.94

Solubility DMSO : ≥ 100 mg/mL; Water : 50 mg/mL 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 bone marrow derived macrophages

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

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BMDMs were stimulated with MSU, GM-CSF/IL-1 β or nigericin $\pm$ fingolimod (2.5 μ M) or febuxostat (200 μ M) and UA levels, ROS, XO, and PP2A activities, Xdh (XO) expression and secreted IL-1 β levels were determined.

Reaction Conditions 2.5 μ M; 3 h

Applications Fingolimod reduced intracellular and secreted UA (catalyzes uric acid) levels, Xdh expression, XO (Xanthine oxidase) activity, ROS (reactive oxygen species) generation and IL-1 β secretion, whereas febuxostat enhanced PP2A (Protein phosphatase 2A) activity.

Animal experiment [2]:

Animal models C57BL6/J mice

Preparation Method Mechanical force-induced HSs were generated in C57BL6/J mice by suturing a dorsal incision and applying a stretching device on Days 6, 8, 10, and 12. On Days 8, 10, and 12, intracutaneous Fingolimod (10 μ M) or control vehicle injections were performed. On Day 14, scar tissues and blood were procured and subjected to histology and flow cytometry.

Dosage form 10 μ M; i.c.

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Applications

Flow cytometry showed that Fingolimod decreased the frequencies of macrophages with M2 predominance in the scars but had no effect on total, CD4+, or CD8a+ T cell frequencies. Fingolimod also decreased the vascular endothelial cell frequencies in the scar along with the microvessels, as determined by immunohistochemistry. Compared to the vehicles, Fingolimod treatment significantly reduced the gross scar area and the cross-sectional scar area on histology. On the other hand, Fingolimod tended to reduce white blood cells and significantly reduced the lymphocyte frequencies in the blood.

References:

- [1] Elsayed S, et al. Protein phosphatase 2A regulates xanthine oxidase-derived ROS production in macrophages and influx of inflammatory monocytes in a murine gout model. *Front Pharmacol.* 2022 Nov 17;13:1033520.
- [2] Aoki M, et al. The Immunosuppressant Fingolimod (Fingolimod) for the Treatment of Mechanical Force-Induced Abnormal Scars. *J Immunol Res.* 2020 Jan 7;2020:7057195.

Background

Fingolimod (FTY720), an immunosuppressant agent, usually used in the treatment of multiple sclerosis, also has anticancer actions and can act as an HDACi (Histone deacetylase inhibitors)[1].

In vitro, Fingolimod at 7.5 or 10 μ M, induced a significant reduction in cell viability in D283 and DAOY cultures, also led to a significant increase in the levels of acetylated H3[1]. In vitro, Fingolimod showed cytotoxic antiproliferative effects against androgen-dependent and -independent prostate cancer cells with IC₅₀ ranging from 3.0 ± 0.3 to 6.8 ± 1.7 μ M[2]. Jurkat T-lymphocytes exposure to Fingolimod suppressed the amplitude of delayed-rectifier K⁺ current (I_{K(DR)}) in a time- and concentration-dependent manner with an IC₅₀ value of 1.51 μ M[3]. Fingolimod reduced the proliferation and viability of Ph(+) and Ph(-) ALL cell lines and patient samples with IC₅₀ values for viability between 5.3 to 7.9 μ M[4]. Fingolimod differentially suppressed the viability of the OSCC cell lines SCC4, SCC25, and SCC2095 with IC₅₀ values of 6.1, 6.3, and 4.5 μ M, respectively[5].

In vivo, E13 C57BL/6 wildtype mice were treated with 1 mg/kg significantly increased the survival of DCX+ neurons in the DG (dentate gyrus) and the SVZ (the subventricular zone) 4 weeks after

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irradiation as well as a slight increase of proliferating cells[6]. In vivo, 5xFAD mice were treated with 1 mg/kg/day fingolimod decreased both peripheral blood lymphocyte counts and brain A β levels, but treated with 0.03 mg/kg/day improved memory, decreased activation of brain microglia and astrocytes, and restored hippocampal levels of GABA and glycerophosphocholine with no effect on circulating lymphocyte counts[7]. In vivo, C57BL/6JOLaHsd mice were treated with 0.5 mg/kg fingolimod increased lesion size (stroke) but decreased ipsilateral brain atrophy in younger mice, without an effect on behavioural outcomes[8].

References:

- [1] Perla AS, et al. Fingolimod (Fingolimod) reduces viability and survival and increases histone H3 acetylation in medulloblastoma cells. *Pediatr Hematol Oncol*. 2020 Mar;37(2):170-175.
- [2] Allam RM, et al. Fingolimod interrupts the cross talk between estrogen metabolism and sphingolipid metabolism within prostate cancer cells. *Toxicol Lett*. 2018 Jul;291:77-85.
- [3] Chang WT, et al. Actions of Fingolimod (Fingolimod), a Sphingosine-1-Phosphate Receptor Modulator, on Delayed-Rectifier K⁺ Current and Intermediate-Conductance Ca²⁺-Activated K⁺ Channel in Jurkat T-Lymphocytes. *Molecules*. 2020 Oct 2;25(19):4525.
- [4] Wallington-Beddoe CT, et al. Fingolimod produces caspase-independent cell death of acute lymphoblastic leukemia cells. *Autophagy*. 2011 Jul;7(7):707-15.
- [5] Bai LY, et al. Fingolimod Induces Autophagy-Associated Apoptosis in Human Oral Squamous Carcinoma Cells, in Part, through a Reactive Oxygen Species/Mcl-1-Dependent Mechanism. *Sci Rep*. 2017 Jul 17;7(1):5600.
- [6] Metzdorf J, et al. Fingolimod for Irradiation-Induced Neurodegeneration. *Front Neurosci*. 2019 Jul 9;13:699.
- [7] Carreras I, et al. Dual dose-dependent effects of fingolimod in a mouse model of Alzheimer's disease. *Sci Rep*. 2019 Jul 29;9(1):10972.
- [8] Diaz Diaz AC, et al. Preclinical Evaluation of Fingolimod in Rodent Models of Stroke With Age or Atherosclerosis as Comorbidities. *Front Pharmacol*. 2022 Jul 13;13:920449.

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