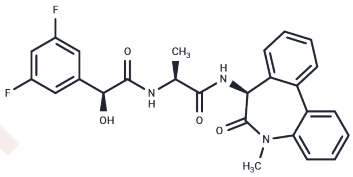
Data Sheet (Cat.No.T6063)

TargetMol

LY-411575

Chemical Properties



CAS No. : 209984-57-6

Formula: C26H23F2N3O4

Molecular Weight: 479.48

Storage: Keep away from moisture,Keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	LY-411575, a potent γ-secretase inhibitor, is with IC50 of 0.078 nM in the membrane and 0.082 nM in cell-based. It also suppresses Notch clevage with IC50 of 0.39 nM.
Targets(IC50)	Apoptosis,Gamma-secretase
In vitro	LY-411575 inhibits γ-secretase which can be assessed by the substrates like amyloid precursor protein (APP) and Notch S3 cleavage. [1] LY-411575, which blocks Notch activation, results in apoptosis in primary and immortalized KS cells. [2]
In vivo	10 mg/kg oral dose of LY-411575 decreases brain and plasma Aβ40 and -42 dose-dependently. [1] LY-411575 reduces cortical Aβ40 in young (preplaque) transgenic CRND8 mice (ED50 ≈ 0.6 mg/kg) and produces significant thymus atrophy and intestinal goblet cell hyperplasia at higher doses (>3 mg/kg). The therapeutic window is similar after oral and subcutaneous administration and in young and aged CRND8 mice. Both the thymus and intestinal side effects are reversible after a 2-week washout period. Three-week treatment with 1 mg/kg LY411575 reduces cortical Aβ40 by 69% without inducing intestinal effects, although a previously unreported change in coat color is observed. [3]
Kinase Assay	Assays for Aβ and NICD: Procedures for measuring γ-secretase activity in membranes prepared from HEK293 cells expressing APP have been described previously (Zhang L et al Biochemistry 40, 5049-5055). Intact HEK293 cells expressing either APP or NΔE are treated with various concentrations of LY- 411,575 for 4 hours at 37 °C. In the case of cells expressing NΔE, cells are lysed, the cell lysates are separated on a 4-12% NuPAGE gel, and the processed NICD fragment is detected via Western blot with a cleavage site-specific antibody. The inhibition of NICD production is quantified by spot densitometric analysis using FluorChem. In the case of cells expressing APP, the conditioned medium is collected, centrifuged at 10,000 × g for 5 minutes to remove cell debris, and stored at -20 °C prior to the determination of Aβ levels. Aβ40 and -42 produced in HEK293 membrane- and cell-based assays, as well as plasma Aβ40 and cortex Aβ40 from TgCRND8 mice, are analyzed without pretreatment using an electrochemiluminescence detection-based immunoassay. Plasma Aβ42 is measured by enzyme-linked immunosorbent assay. A commercially available enzyme-linked immunosorbent assay kit is used to measure cortex Aβ42 according to the manufacturer''s instructions.

Cell Research	DNA/PI staining is performed using standard methodologies. Briefly, 1 × 106 cells are permeabilized with 100% ethanol in the presence of 15% FBS. The cells are washed and then treated for 15 minutes at 37 °C with 10 mg/mL RNAse. PI (5 mg/mL) is added, and the cells incubated for 1 hour at 4 °C prior to analysis by flow cytometry with 10 000 cells analysed per gated determination. The results are confirmed using the Immunotech Annexin V staining kit following the manufacturers' instructions. At least three independent experiments are performed showing similar results.</(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 35.71 mg/mL (74.48 mM),Sonication is recommended. Ethanol: 11 mg/mL (22.94 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (6.88 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0856 mL	10.428 mL	20.8559 mL
5 mM	0.4171 mL	2.0856 mL	4.1712 mL
10 mM	0.2086 mL	1.0428 mL	2.0856 mL
50 mM	0.0417 mL	0.2086 mL	0.4171 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Wong GT, et al, J Biol Chem, 2004, 279(13), 12876-12882.
Yang D L, Zhang Y, He L, et al. Demethylzeylasteral (T-96) Initiates Extrinsic Apoptosis Against Prostate Cancer cells by Inducing ROS-Mediated ER Stress and Suppressing Autophagic Flux. Biological Research. 2021, 54(1): 1-14.
Zhang S, Lou H, Lu H, et al.Characterization of Proliferation Medium and Its Effect on Differentiation of Muscle Satellite Cells from Larimichthys crocea in Cultured Fish Meat Production.Fishes.2023, 8(9): 429.
Curry CL, et al, Oncogene, 2005, 24(42), 6333-6344.
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Lou H, Lu H, Zhang S, et al.Highly aligned myotubes formation of piscine satellite cells in 3D fibrin hydrogels of cultured meat.International Journal of Biological Macromolecules.2024: 136879.
Yang D L, Zhang Y, He L, et al. Demethylzeylasteral (T-96) Initiates Extrinsic Apoptosis Against Prostate Cancer cells by Inducing ROS-Mediated ER Stress and Suppressing Autophagic Flux[J]. 2021

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