

LY-411575

Chemical Properties

CAS No. : 209984-57-6

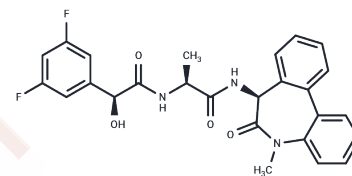
Formula: C₂₆H₂₃F₂N₃O₄

Molecular Weight: 479.48

Appearance: no data available

Storage: keep away from moisture, keep away from direct sunlight

Powder: -20°C for 3 years | In solvent: -80°C for 1 year



Biological Description

Description	LY-411575, a potent γ -secretase inhibitor, is with IC ₅₀ of 0.078 nM in the membrane and 0.082 nM in cell-based. It also suppresses Notch cleavage with IC ₅₀ of 0.39 nM.
Targets(IC ₅₀)	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 A β ₄₀ and -42 dose-dependently. [1] LY-411575 reduces cortical A β ₄₀ in young (preplaque) transgenic CRND8 mice (ED ₅₀ \approx 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 A β ₄₀ by 69% without inducing intestinal effects, although a previously unreported change in coat color is observed. [3]
Kinase Assay	Assays for A β 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 N Δ E are treated with various concentrations of LY- 411,575 for 4 hours at 37 °C. In the case of cells expressing N Δ E, 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 \times g for 5 minutes to remove cell debris, and stored at -20 °C prior to the determination of A β levels. A β ₄₀ and -42 produced in HEK293 membrane- and cell-based assays, as well as plasma A β ₄₀ and cortex A β ₄₀ from TgCRND8 mice, are analyzed without pretreatment using an electrochemiluminescence detection-based immunoassay. Plasma A β ₄₂ is measured by enzyme-linked immunosorbent assay. A commercially available enzyme-linked immunosorbent assay kit is used to measure cortex A β ₄₂ according to the manufacturer's instructions.

Cell Research	DNA/PI staining is performed using standard methodologies. Briefly, 1×10^6 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)
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Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 88 mg/mL (183.53 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)
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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.

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.

Hyde LA, et al, J Pharmacol Exp Ther, 2006, 319(3), 1133-1143.

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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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