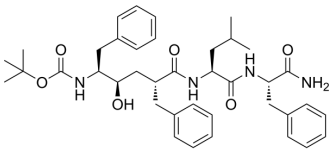
L-685458

Cat. No.:	HY-19369
CAS No.:	292632-98-5
Molecular Formula:	$C_{39}H_{52}N_4O_6$
Molecular Weight:	672.85
Target:	γ-secretase; Apoptosis
Pathway:	Neuronal Signaling; Stem Cell/Wnt; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 83.3 mg/mL (123.80 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4862 mL	7.4311 mL	14.8622 mL
	5 mM	0.2972 mL	1.4862 mL	2.9724 mL
	10 mM	0.1486 mL	0.7431 mL	1.4862 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

L-685458 is a potent transition state analog (TSA) γ-secretase inhibitor (GSI). L-685458 inhibits amyloid β-protein precursor γ-secretase activity with IC_{50} of 17 nM, shows greater than 50-100-fold selectivity over other aspartyl proteases tested. L685458 inhibits γ-secretase-mediated cleavage of APP-C99 and Notch-100 with IC_{50}s of 301.3 nM and 351.3 nM, respectively. L-685458 can be used for the research of alzheimer's disease (AD) and cancers[1][2].

In Vitro

L-685458 reduces both Aβ(40) and Aβ(42) peptide formation in 3 different cells. It against Neuro2A h AβPP695, CHO h Aβ PP695, and SHSY5 spβA4CTF reduction of Aβ(40) with IC_{50} values of 402 nM, 113 nM and 48 nM, respectively. And the IC_{50} values are 775 nM, 248 nM, 67 nM, respectively[1].

L-685458 (5-40 μM; 24 hours) leads to a dramatic downregulation of Hes-1 in 786-O cells[3].

L-685458 has inhibitory effects in hepatoma cell lines, it against Huh7, HepG2, HLE and SKHep1 cells with IC_{50} of 12.91 μM, 12.69 μM, 21.76 μM and 12.18 μM, respectively[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

L-685458 (percutaneous administration; 5 mg/kg; 2 weeks) has antitumor effects in mouse hepatoma models. L-685458 inhibits EpCAM production except in necrotic areas. And HES1 staining is also diminished in the nucleus[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	NOD-SCID Mouse Hepatoma Model[4]
Dosage:	5 mg/kg
Administration:	Percutaneous administration; 5 mg/kg; 2 weeks
Result:	Exhibited anti-tumor activities in vivo.

CUSTOMER VALIDATION

- Cell. 2021 Jan 21;184(2):521-533.e14.
- Cell Rep. 2022 May 24;39(8):110857.
- Evid Based Complement Alternat Med. 2018 Nov 21;2018:3082507.

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REFERENCES

[1]. Shearman, M.S., Beher, D., Clarke, E.E., Lewis, H.D., Harrison, T., Hunt, P.,

[2]. Guanghui Yang, et al. Structural basis of γ-secretase inhibition and modulation by small molecule drugs. Cell. 2021 Jan 21;184(2):521-533.e14.

[3]. Jonas Sjölund, et al. Suppression of renal cell carcinoma growth by inhibition of Notch signaling in vitro and in vivo. J Clin Invest. 2008 Jan;118(1):217-28.

[4]. Kazunori Kawaguchi, et al. Jagged1 DNA Copy Number Variation Is Associated with Poor Outcome in Liver Cancer. Am J Pathol. 2016 Aug;186(8):2055-2067.

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