Laduviglusib

Cat. No.: HY-10182

CAS No.: 252917-06-9

Molecular Formula: $C_{22}H_{18}Cl_2N_8$

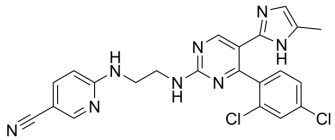
Molecular Weight: 465.34

Target: GSK-3; Autophagy; Wnt; β-catenin; Organoid

Pathway: PI3K/Akt/mTOR; Stem Cell/Wnt; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 16.67 mg/mL (35.82 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1490 mL	10.7448 mL	21.4897 mL
	5 mM	0.4298 mL	2.1490 mL	4.2979 mL
	10 mM	0.2149 mL	1.0745 mL	2.1490 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 5 mg/mL (10.74 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 20% SBE-β-CD in Saline adjusted to pH 4-4.5 with 1 N Acetic
   Solubility: 5 mg/mL (10.74 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.47 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Laduviglusib (CHIR-99021) is a potent, selective and orally active GSK-3α/β inhibitor with IC_{50}s of 10 nM and 6.7 nM. Laduviglusib shows >500-fold selectivity for GSK-3 over CDC2, ERK2 and other protein kinases. Laduviglusib is also a potent Wnt/β-catenin signaling pathway activator. Laduviglusib enhances mouse and human embryonic stem cells self-renewal. Laduviglusib induces autophagy[1][2][3].

IC_{50} & Target	GSK-3β	GSK-3α	cdc2
	6.7 nM (IC_{50})	10 nM (IC_{50})	8800 nM (IC_{50})

In Vitro

Laduviglusib (1-10 μM, 3 days) reduces the viability of the ES-D3 cells with an IC_{50} of 4.9 μM[2].
Laduviglusib (5 μM, 48 h) activates the canonical Wnt-pathway in ES-D3 cells and ES-CCE cells[2].
Laduviglusib (3 μM, 4 days) inhibits ES cell differentiation into neural cells[3].
Laduviglusib (1 μM, 2 weeks) inhibits adipogenesis by blocking induction of C/EBPα and PPARγ in 3T3-L1 preadipocytes[4].
Laduviglusib (2.5 μM, 24 h) protects Lgr5+ cells against radiation-induced apoptosis[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	ES-D3 cells
Concentration:	1-10 μM
Incubation Time:	3 days
Result:	Reduced the viability of the ES-D3 cells by 24.7% at 2.5 μM, 56.3% at 5 μM, 61.9% at 7.5 μM and 69.2% at 10 μM

In Vivo

Laduviglusib (30 mg/kg, p.o) rapidly lowers plasma glucose[1].
Laduviglusib (2 mg/kg, i.p.) protects mice against radiation-induced lethal GI injury[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	ZDF rats[1]
Dosage:	30 mg/kg
Administration:	Oral administration
Result:	Lowered plasma glucose, with a maximal reduction of nearly 150 mg/dl 3-4 h after administration.

Animal Model:	WT C57BL/6 mice[5]
Dosage:	2 mg/kg
Administration:	Intraperitoneal injection (i.p.)
Result:	Blocked crypt apoptosis and increased Lgr5+ cell survival.

CUSTOMER VALIDATION

- Nat Med. 2016 May;22(5):547-56.
- Mol Cancer. 2024 Jan 10;23(1):12.
- Cell Discov. 2023 Jun 6;9(1):53.
- Nat Genet. 2024 Feb;56(2):294-305.
- Cell Metab. 2024 Jun 18:S1550-4131(24)00189-X.

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REFERENCES

[1]. Ring DB, et al. Selective glycogen synthase kinase 3 inhibitors potentiate activation of glucose transport and utilization in vitro and in vivo. Diabetes. 2003 Mar;52(3):588-95.

[2]. Bennett CN, et al. Regulation of Wnt signaling during adipogenesis. J Biol Chem. 2002 Aug 23;277(34):30998-1004.

[3]. Naujok O, et al. Cytotoxicity and activation of the Wnt/beta-catenin pathway in mouse embryonic stem cells treated with four GSK3 inhibitors.BMC Res Notes. 2014 Apr 29;7:273.

[4]. Wang X, et al. Pharmacologically blocking p53-dependent apoptosis protects intestinal stem cells and mice from radiation. Sci Rep. 2015 Apr 10;5:8566.

[5]. Ye S, et al. Pleiotropy of glycogen synthase kinase-3 inhibition by CHIR99021 promotes self-renewal of embryonic stem cells from refractory mouse strains. PLoS One. 2012;7(4):e35892.

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