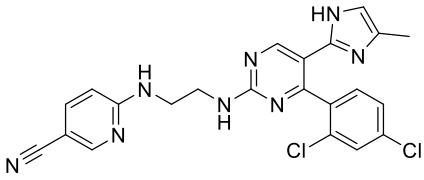
Product data sheet

MedKoo Cat#: 200774 Name: CHIR-99021 CAS#: 252917-06-9 (free base) Chemical Formula: $C_{22}H_{18}Cl_2N_8$ Exact Mass: 464.10315 Molecular Weight: 465.34	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
CHIR-99021, also known as CT99021, is a glycogen synthase kinase 3β (GSK3β) inhibitor that has antiproliferative activity in vitro and in vivo. CHIR-99021 inhibits GSK-3 with IC50 at 7 nM. In a series of carcinoma cell lines, the IC50 of CHIR99021 for proliferation is about 10μM.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	9.49	20.40
Ethanol	47.0	101.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.15 mL	10.74 mL	21.49 mL
5 mM	0.43 mL	2.15 mL	4.30 mL
10 mM	0.21 mL	1.07 mL	2.15 mL
50 mM	0.04 mL	0.21 mL	0.43 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Delepine C, Pham VA, Tsang HWS, Sur M. GSK3ß inhibitor CHIR 99021 modulates cerebral organoid development through dose-dependent regulation of apoptosis, proliferation, differentiation and migration. PLoS One. 2021 May 5;16(5):e0251173. doi: 10.1371/journal.pone.0251173. PMID: 33951093; PMCID: PMC8099055.
2. Lee JS, Chae MK, Kikkawa DO, Lee EJ, Yoon JS. Glycogen Synthase Kinase-3β Mediates Proinflammatory Cytokine Secretion and Adipogenesis in Orbital Fibroblasts from Patients with Graves' Orbitopathy. Invest Ophthalmol Vis Sci. 2020 Jul 1;61(8):51. doi: 10.1167/iovs.61.8.51. PMID: 32735324; PMCID: PMC7426624.

In vivo study

1. Faccidomo S, Holstein SE, Santanam TS, Saunders BL, Swaim KS, Reid GT, O'Neill C, Eastman VR, Hodge CW. Pharmacological inhibition of glycogen synthase kinase 3 increases operant alcohol self-administration in a manner associated with altered pGSK-3β, protein interacting with C kinase and GluA2 protein expression in the reward pathway of male C57BL/6J mice. Behav Pharmacol. 2020 Feb;31(1):15-26. doi: 10.1097/FBP.0000000000000501. PMID: 31503067; PMCID: PMC6954298.
2. Badimon L, Casaní L, Camino-Lopez S, Juan-Babot O, Borrell-Pages M. GSK3β inhibition and canonical Wnt signaling in mice hearts after myocardial ischemic damage. PLoS One. 2019 Jun 20;14(6):e0218098. doi: 10.1371/journal.pone.0218098. PMID: 31220102; PMCID: PMC6586285.

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7. Bioactivity

Biological target:

CHIR-99021 (CT99021) is a potent and selective GSK-3α/β inhibitor with IC50s of 10 nM and 6.7 nM.

In vitro activity

Organoids treated with low dose of CHIR 99021 (1μM) showed increased levels of neural progenitor cell (NPC) markers SOX2 (WB, 1.5-fold increase) and PAX6 (IHC, 1.8-fold increase), and of radial glia marker BLBP (WB, 2.1-fold increase). No change was observed for levels of neuroepithelium marker E-cadherin and neuronal markers TUJ1 and DCX. In contrast, organoids treated with 10μM CHIR 99021 showed increased levels of E-cadherin (WB and IHC, 1.8-fold and 92-fold increase) and of intermediate progenitor marker TBR2 (2.9-fold increase), decreased levels of NPC markers SOX2 (WB, 1.9-fold decrease) and PAX6 (IHC, 2-fold decrease), and decreased levels of neuronal marker DCX (IHC, 7.8-fold decrease). This suggests that GSK3β signaling modulates neuroepithelium differentiation in a dose dependent manner.

Reference: PLoS One. 2021; 16(5): e0251173. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8099055/

In vivo activity

Phosphorylated GSK3β (p-GSK3β, Tyr216) protein levels were higher in ischemic regions of hearts from Lrp5-/- mice than in those from Wt mice (Fig 1A). Total GSK3β protein levels were also increased in the myocardium of Lrp5-/- mice compared to Wt mice. Phosphorylated GSK3β/Total- GSK3β ratios to analyze total myocardial content of activated GSK3β found no differences between genotypes (Fig 1A). CHIR99021 treatment significantly reduced p-GSK3β protein levels in Lrp5-/- mice but not in Wt mice. CHIR99021 treatment reduced p-GSK3β to the same level in both genotypes. Induction of myocardial injury (MI) causes a highly significant increase of p-GSK3β protein levels in Wt and Lrp5-/- mice, strongly suggesting that injury affects the canonical Wnt pathway (Fig 1B). Treatment with CHIR99021 before occlusion significantly reduced p-GSK3β levels in both genotypes (Fig 1C) further demonstrating efficacy of CHIR99021 treatments. Indeed, levels of p-GSK3β protein were significantly reduced after CHIR99021 treatments in damaged hearts leaving the canonical pathway open for activation and for β-catenin interaction with specific transcription factors.

Reference: PLoS One. 2019; 14(6): e0218098. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6586285/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.