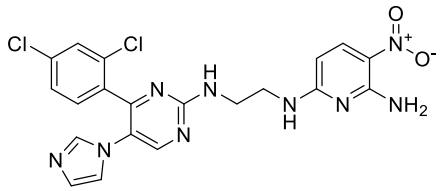
Product data sheet

MedKoo Cat#: 510328 Name: CHIR98014 CAS#: 252935-94-7 Chemical Formula: C20H17Cl2N9O2 Exact Mass: 485.08823 Molecular Weight: 486.31	
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:
CHIR98014, also known as CT-98014, is a reversible, cell-permeable inhibitor of GSK3α and GSK3β (IC50 = 0.65 and 0.58 nM, respectively). It is inactive against a series of other serine/threonine or tyrosine kinases. Through its effects on GSK3, CHIR98014 stimulates glycogen synthase in cells (EC50 = 106 nM), potentiates insulin-dependent glucose transport in isolated muscle strips, and improves glucose disposal in diabetic animals. CHIR98014 also reduces tau phosphorylation in rat brains and supports Wnt signaling during osteogenesis.

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	13.24	27.23
DMSO:PBS (pH 7.2) (1:4)	0.2	0.41
DMF	1.0	2.06

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.06 mL	10.28 mL	20.56 mL
5 mM	0.41 mL	2.06 mL	4.11 mL
10 mM	0.21 mL	1.03 mL	2.06 mL
50 mM	0.04 mL	0.21 mL	0.41 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. Ocasio JK, Bates RDP, Rapp CD, Gershon TR. GSK-3 modulates SHH-driven proliferation in postnatal cerebellar neurogenesis and medulloblastoma. Development. 2019 Oct 10;146(20):dev177550. doi: 10.1242/dev.177550. PMID: 31540917; PMCID: PMC6826032.
2. Qiu YS, Jiang NN, Zhou Y, Yu KY, Gong HY, Liao GJ. LMO3 promotes gastric cancer cell invasion and proliferation through Akt-mTOR and Akt-GSK3β signaling. Int J Mol Med. 2018 May;41(5):2755-2763. doi: 10.3892/ijmm.2018.3476. Epub 2018 Feb 8. PMID: 29436606; PMCID: PMC5846634.

In vivo study

1. Liu H, Zhu J, Mao Z, Zhang G, Hu X, Chen F. Tuft1 promotes thyroid carcinoma cell invasion and proliferation and suppresses apoptosis through the Akt-mTOR/GSK3β signaling pathway. Am J Transl Res. 2018 Dec 15;10(12):4376-4384. PMID: 30662679; PMCID: PMC6325505.

2. Selenica ML, Jensen HS, Larsen AK, Pedersen ML, Helboe L, Leist M, Lotharius J. Efficacy of small-molecule glycogen synthase kinase-3 inhibitors in the postnatal rat model of tau hyperphosphorylation. Br J Pharmacol. 2007 Nov;152(6):959-79. doi: 10.1038/sj.bjp.0707471. Epub 2007 Oct 1. PMID: 17906685; PMCID: PMC2078230.

7. Bioactivity

Biological target:

CHIR-98014 is a potent, cell-permeable GSK-3 inhibitor with IC50s of 0.65 and 0.58 nM for GSK-3α and GSK-3β, respectively; it shows less potent activities against cdc2 and erk2.

In vitro activity

CHIR98 produced dose-dependent reductions of both p-CTNNB (phosphorylated Catenin Beta 1) and p-RB (phosphorylated retinoblastoma), reducing p-RB in SHH (sonic hedgehog)-treated CGNPs (cerebellar granule neuron progenitors) as effectively as SHH deprivation (Fig. 3B). GSK-3 inhibition through CHIR98 increased CDKN1A protein levels in CGNPs compared with controls (Fig. 3B). The decrease in proliferation was not accompanied by increased apoptosis, as CHIR98 did not induce a significant or dose-related increase in cC3 (cleaved caspase-3) (Fig. 3B). In parallel cellular quantifications, we found that CHIR98 reduced the number cells showing p-RB expression, EdU (5-ethynyl-2'-deoxyuridine) incorporation and p-HH3 (histone H3) expression, and fewer cells were observed in S phase and M phase compared with SHH-treated controls (Fig. 3C,D). Treatment of CGNPs with the GSK-3 inhibitors LY2090314 (LY209), AZD1080 or LiCl did not decrease p-RB or p-HH3 levels or reduce EdU incorporation as effectively as CHIR98 at similar concentrations (Fig. S2). These results show that modulation of SHH-driven proliferation by GSK-3 is seen outside of the context of genetic deletion and can be achieved within the dynamic range of physiological GSK-3 activity.

Reference: Development. 2019 Oct 15; 146(20): dev177550. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6826032/

In vivo activity

P12 rats were injected i.v. with 30 mg kg−1 of the compound dissolved in DMSO. Different doses, vehicles and routes of administration were tested and brain exposure studies were performed (see Methods section and Table 1). Dissolving the compound in DMSO and injecting it i.v. led to a maximal concentration in the brain of 7 μm (Table 2). Animals were therefore treated i.v. with 30 mg kg−1 CHIR98014 for 1, 2 and 4 h. As shown in Table 1, accumulation of CHIR98014 in the brain reached a peak after 1 h and remained stable even after 2 and 4 h of injection. Tissue analysed by western blotting using a Ser396 p-tau antibody showed a ≈40% reduction in the phosphorylation of 43 and 49 kDa tau in the cortex (Figures 7a–c). A significant, threefold reduction in the 43 kDa isoform was also observed in the hippocampus (Figures 7d and e), while no significant reduction in 49 kDa was observed at any time point (Figures 7d and f). Furthermore, a dose-dependent decrease in p-tau levels was also observed when CHIR98014 was injected i.v. for 1 h at different doses (1–30 mg kg−1) although a significant reduction was only detectable at doses above 10 mg kg−1 (Figures 8a–c). The potency of CHIR98014 correlated well with its maximal brain concentration (7 μm) and IC50 for this compound (3.7 nm, Table 2). At 2 μm, CHIR98014 led to a >90% reduction in p-tau in a human neuronal cell line (Table 2).

Reference: Br J Pharmacol. 2007 Nov; 152(6): 959–979. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2078230/

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.