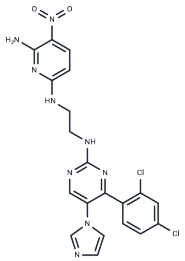
Data Sheet (Cat.No.T2608)

TargetMol

CHIR-98014

Chemical Properties



CAS No. : 252935-94-7

Formula: C20H17Cl2N9O2

Molecular Weight: 486.31

Appearance: no data available

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

Biological Description

Description	CHIR-98014 (CT98014) is a selective GSK3 inhibitor; potentiate insulin activation of glucose transport and utilization in vitro and in vivo.
Targets(IC50)	FGFR,GSK-3,S6 Kinase,Src
In vitro	CHIR 98014 demonstrates significant efficacy in reducing hyperglycemia and enhancing glucose utilization not only in db/db mice and ZDF rats but also in ob/ob mice, diet-induced diabetic C57BL/6 mice, and glucose intolerant SHHF rats treated with CHIR-2, indicating its broad applicability across various diabetes models. Furthermore, CHIR-98014 reduces the phosphorylation of tau protein (Ser396) in the cortex and hippocampus of postnatal rats. As a GSK-3 inhibitor, CHIR-98014 activates glycogen synthase (GS) activity in type I skeletal muscle isolated from lean diabetic and insulin-resistant ZDF rats. Insulin together with CHIR 98014 induces a stronger activation of GS in muscles isolated from lean diabetic rats compared to those from ZDF rats, yet neither CHIR 98014 nor insulin alone modifies the total GS activity in these cells and muscles. Additionally, CHIR 98014 does not alter the insulin dose-response in muscles isolated from lean animals.
In vivo	CHIR-98014 acts as a simple competitive inhibitor binding to ATP, displaying selectivity for GSK-3 that is 500 to >1000 times greater than that for 20 other protein kinases, including Cdc2, ERK2, Tie-2, and KDR. It inhibits human GSK-3β with a Ki value of 0.87 nM and CDC2 with an IC50 of 3.7 μM. CHIR-98014 similarly affects the highly homologous α and β isoforms of GSK-3, yet distinctly differs between GSK-3 and its closest homologs, cdc2 and erk2. Exposure of CHO-IR cells, expressing insulin receptors, or primary rat hepatocytes to increasing concentrations of CHIR-98014 resulted in a stimulation of GS activity to levels two to three times above baseline, with half-maximal GS stimulation response concentrations of 106 and 107 nM, respectively.
Kinase Assay	Kinase assays: Polypropylene 96-well plates are ?lled with 300 μL/well buffer (50 mM tris HCl, 10 mM MgCl2, 1 mM EGTA, 1 mM dithiothreitol, 25 mM β-glycerophosphate, 1 mM NaF, 0.01% BSA, pH 7.5) containing kinase, peptide substrate, and any activators. CHIR-98014 or controls are added in 3.5 μL of DMSO, followed by 50 μL of ATP stock to yield a ?nal concentration of 1 μM ATP in all cell-free assays. After incubation, triplicate 100-μL aliquots are transferred to Combiplate eight plates containing 100 μL/well 50 μM ATP and 20 mM EDTA. After 1 hour, the wells are rinsed ?ve times with PBS, ?lled with 200 μL of scintillation ?uid, sealed, left 30 min, and counted in a scintillation counter. All steps are performed at room temperature.

Cell Research	CHO-IR cells expressing human insulin receptor are grown to 80% con?uence in Hamm's F12 medium with 10% fetal bovine serum and without hypoxanthine. Trypsinized cells are seeded in 6-well plates at 1 × 106 cells/well in 2 mL of medium without fetal bovine serum. After 24 hours, medium is replaced with 1 mL of serum-free medium containing GSK-3 inhibitor CHIR 98014 or control (?nal DMSO concentration 0.1%) for 30 min at 37 °C. Cells are lysed by freeze/thaw in 50 mM tris (pH 7.8) containing 1 mM EDTA, 1 mM DTT, 100 mM NaF, 1 mM phenylmethylsulfonyl ?uoride, and 25 μg/mL leupeptin (buffer A) and centrifuged 15 min at 4 °C/14000 g. The activity ratio of GS is calculated as the GS activity in the absence of glucose-6-phosphate divided by the activity in the presence of 5 mM glucose-6-phosphate. (Only for Reference)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 4.86 mg/mL (10 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0563 mL	10.2815 mL	20.563 mL
5 mM	0.4113 mL	2.0563 mL	4.1126 mL
10 mM	0.2056 mL	1.0282 mL	2.0563 mL
50 mM	0.0411 mL	0.2056 mL	0.4113 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

Ring DB,et al. Diabetes. 2003, 52(3), 588-595.
Selenica ML, et al. Br J Pharmacol. 2007, 152(6), 959-979.