

Product Data Sheet

Product Name: CHIR-98014

Cat. No.: GC12176

Chemical Properties

Cas. No. 252935-94-7

Chemical Name 6-N-[2-[[4-(2,4-dichlorophenyl)-5-imidazol-1-yl]pyrimidin-2-yl]amino]ethyl]-3-nitropyridine-2,6-diamine

SMILES C1=CC(=C(C=C1Cl)Cl)C2=NC(=NC=C2N3C=CN=C3)NCCNC4=NC(=C(C=C4)[N+](=O)[O-])N

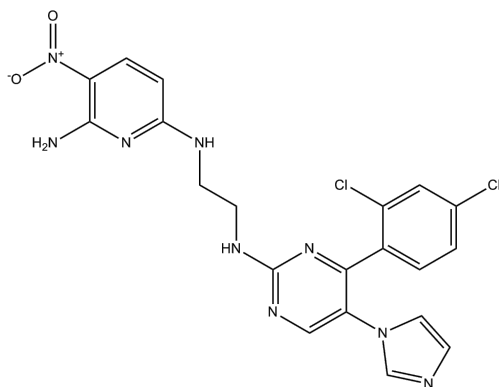
Formula $C_{20}H_{17}Cl_2N_9O_2$ M.Wt 486.31

Solubility $\geq 8.1\text{mg/mL}$ in DMSO with gentle warming Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell experiment [1]:

Cell lines Cortical and hippocampal neurons

Preparation Method To stabilize the microtubule cytoskeleton, cells were pretreated with the GSK-3 inhibitor CHIR-98014 (10 μ M) for 1h and then incubated in the presence or absence of 20 μ M PrP1-30 for 12h. Confocal microscopy was used to observe cortical and hippocampal neurons.

Reaction
Conditions 10 μ M; 1h

Applications Treatment of the cortical as well as hippocampal neurons with 10 μ M CHIR-98014 prevents loss of neurites caused by 20 μ M PrP1-30.

Animal experiment [2]:

Animal models Male CB17-SCID mice

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Male CB17-SCID mice were inoculated with HepG2 cells subcutaneously to establish HepG2 mice subcutaneously transplanted tumor models. Twenty-three days after inoculation, the tumor-bearing mice were divided into 3 groups according to the size of the tumor by the random block method, with 3 mice in each group: CHIR-98014 (10mg/kg) group, Hjp-6-171 (50mg/kg) group and the Preparation Method drug combination group (CHIR-98014 10mg/kg+Hjp-6-171 50mg/kg). Average tumor volume in each group after grouping was about 194mm³. Each group was administered by daily intragastric administration of corresponding inhibitors at a dose of 10mL/kg for 15 days. At the end of the experiment, animals were euthanized with CO₂, and subcutaneous tumor tissues were quickly stripped and weighed.

Dosage form 10mg/kg; 15 days; p.o.

Applications Either treatment with Hjp-6-171 or CHIR-98014 alone could inhibit tumor growth in vivo, combination therapy had a synergistic effect.

References:

- [1] Zajkowski T, Nieznanska H, Nieznanski K. Stabilization of microtubular cytoskeleton protects neurons from toxicity of N-terminal fragment of cytosolic prion protein[J]. Biochimica et Biophysica Acta (BBA)-Molecular Cell Research, 2015, 1853(10): 2228-2239.
- [2] Liu Y, Xue M, Cao D, et al. Multi-omics characterization of WNT pathway reactivation to ameliorate BET inhibitor resistance in liver cancer cells[J]. Genomics, 2021, 113(3): 1057-1069.

Background

CHIR-98014 is a potent, cell-permeable inhibitor of GSK-3 α and GSK-3 β with IC₅₀ values of 0.65nM and 0.58nM, respectively^[1]. GSK-3 (glycogen synthase kinase 3) is a serine/threonine protein kinase and plays a key role in many central intracellular signaling pathways, including cell proliferation,

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migration, inflammation and immune response, glucose regulation, and apoptosis^[2, 3]. CHIR-98014 can regulate the Wnt/ β -catenin signaling pathway and has a wide range of applications in stem cell maintenance, metabolic diseases, and neurodegenerative disease research^[4].

In vitro, pretreatment of cortical and hippocampal neurons with CHIR-98014 (10 μ M) for 1h significantly reduced PrP1-30-induced neurite loss and significantly reduced the number of dead cells^[5]. Treatment of A549 cells with CHIR-98014 (0.25-2 μ M) for 48h inhibited phosphorylation of Ser46 and Ser392 (p53 activation markers) induced by actinomycin D and Nutlin-3a (A+N), but made the cells sensitive to A+N-induced apoptosis^[6].

In vivo, oral treatment of HepG2 liver cancer cell xenograft mice with CHIR-98014 (10mg/kg) for 15 days significantly inhibited tumor growth in mice, and combined with Hjp-6-171, it exerted a synergistic effect^[7]. Oral treatment of NSG mice with KMT2A rearranged leukemia with CHIR-98014 (15mg/kg) partially inhibited the tumor burden of mice and significantly prolonged the survival of mice^[8].

References:

- [1] Ring D B, Johnson K W, Henriksen E J, et al. Selective glycogen synthase kinase 3 inhibitors potentiate insulin activation of glucose transport and utilization in vitro and in vivo[J]. Diabetes, 2003, 52(3): 588-595.
- [2] Pan W A, Tsai H Y, Wang S C, et al. The RNA recognition motif of NIFK is required for rRNA maturation during cell cycle progression[J]. RNA biology, 2015, 12(3): 255-267.
- [3] Joep R S, Yuskaitis C J, Beurel E. Glycogen synthase kinase-3 (GSK3): inflammation, diseases, and therapeutics[J]. Neurochemical research, 2007, 32: 577-595.
- [4] Phukan S, Babu V S, Kannoji A, et al. GSK3 β : role in therapeutic landscape and development of modulators[J]. British journal of pharmacology, 2010, 160(1): 1-19.
- [5] Zajkowski T, Nieznanska H, Nieznanski K. Stabilization of microtubular cytoskeleton protects neurons from toxicity of N-terminal fragment of cytosolic prion protein[J]. Biochimica et Biophysica Acta (BBA)-Molecular Cell Research, 2015, 1853(10): 2228-2239.
- [6] Łasut-Szyszk B, Małachowska B, Gdowicz-Kłosok A, et al. Transcriptome Analysis of Cells exposed to actinomycin D and Nutlin-3a reveals new candidate p53-Target genes and indicates that CHIR-98014 is an important inhibitor of p53 activity[J]. International Journal of Molecular Sciences, 2021, 22(20): 11072.
- [7] Liu Y, Xue M, Cao D, et al. Multi-omics characterization of WNT pathway reactivation to

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ameliorate BET inhibitor resistance in liver cancer cells[J]. Genomics, 2021, 113(3): 1057-1069.
[8] Wright S, Hu J, Wang H, et al. Interrogating bromodomain inhibitor resistance in KMT2A-rearranged leukemia through combinatorial CRISPR screens[J]. Proceedings of the National Academy of Sciences, 2023, 120(16): e2220134120.

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