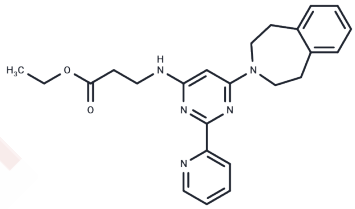
Data Sheet (Cat.No.T3100)

TargetMol

GSK-J4

Chemical Properties



CAS No. : 1373423-53-0

Formula: C24H27N5O2

Molecular Weight: 417.5

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	GSK-J4 (GSK J4 HCl) is a cell permeable prodrug of GSK-J1, a dual inhibitor of the H3K27me3/me2 demethylases JMJD3/KDM6B and UTX/KDM6A (IC50=8.6/6.6 μM). GSK-J4 induces endoplasmic reticulum stress-related apoptosis.
Targets(IC50)	Apoptosis,Histone Demethylase
In vitro	**METHODS**: Prostate cancer cell lines R1-AD1, R1-D567, R1-I567, CWR22Rv-1 and PC3 were treated with GSK-J4 (0-32 μM) for 72 h. Cell viability was measured by Alamar blue reagent. **RESULTS**: GSK-J4 had cell growth inhibitory and/or cytotoxic effects on PC cells. cWR22Rv-1 was the most sensitive to the treatment, with an ED50 of about 3 μM.[1] **METHODS**: Human acute myeloid leukemia cells KG-1a were treated with GSK-J4 (2-10 μM) for 48 h. Apoptosis was detected by Flow cytometry. **RESULTS**: The apoptosis rate of KG-1a cells in the GSK-J4 treatment group was significantly increased compared with the control group. [2]
In vivo	**METHODS**: To investigate the effect on sepsis, GSK-J4 (1-3 mg/kg) was administered intraperitoneally to ICR mice, and sepsis was induced by injection of bacterial suspension 1 h later. **RESULTS**: Pharmacological inhibition of JMJD3 by GSKJ4 protected mice from early septic death and reduced the production of the pro-inflammatory cytokine IL-1β and the expression of IL-6, TNF-α and MCP-1. [3]
Animal Research	GSK-J4 is prepared in DMSO and diluted 1/10 with ethanol.Six-to eight-week-old female C57BL/6 WT mice are injected by subcutaneous injection (s.c.) with 50 μg myelin oligodendrocyte glycoprotein 35-55 peptide (pMOG) emulsified in Complete Freund's Adjuvant (CFA) supplemented with heat-inactivated Mycobacterium tuberculosis H37 RA. In addition, mice receive intraperitoneal injection (i.p.) of 500 ng of pertussis toxin on days 0 and 2. Clinical signs are assessed daily according to the following scoring criteria: 0, no detectable signs; 1, flaccid tail; 2, hind limb weakness or abnormal gait; 3, complete hind limb paralysis; 4, paralysis of fore and hind limbs; and 5, moribund or death. A stock solution of GSK-J4 of 42 mg/mL (100 mM) is prepared in dimethyl sulfoxide (DMSO) to preserve stability. Before injection, the stock solution is diluted 1/10 with ethanol (DMSO: ethanol, 1:10 v/v) and brought to a final concentration of 140 μg/mL in PBS. In systemic drug evaluation experiments, each mouse receive daily i.p. injections (from days 0-5) of 100 μL of this solution containing 14.0 μg of the GSK-J4 (equivalent to 0.56 mg/kg of the drug). Control mice receive 100 μL of the vehicle during

Animal Research	the same period. In other EAE experiments, 106 bone marrow-derived DCs from WT mice are treated with GSK-J4 or vehicle alone for 16 h, pulsed with 5 μg/mL of pMOG for 4 h and then transferred i.v. into WT C57BL/6 recipient mice 14 and 7 days before EAE induction. In other adoptive transfer EAE experiments, CD4+Foxp3+ Treg cells generated in the presence or absence of 25 nM GSK-J4 are purified by cell sorting and then 0.75 ×106 transferred i.v. into WT C57BL/6 recipient mice 1 day before EAE induction.

Solubility Information

Solubility	Ethanol: 41.75 mg/mL (100 mM),Sonication is recommended. DMSO: 141 mg/mL (337.72 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4.18 mg/mL (10.01 mM),Solution. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3952 mL	11.976 mL	23.9521 mL
5 mM	0.479 mL	2.3952 mL	4.7904 mL
10 mM	0.2395 mL	1.1976 mL	2.3952 mL
50 mM	0.0479 mL	0.2395 mL	0.479 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Morozov VM, et al. Inhibitor of H3K27 demethylase JMJD3/UTX GSK-J4 is a potential therapeutic option for castration resistant prostate cancer. Oncotarget. 2017 Jul 8;8(37):62131-62142.

Zheng B, Liu J, Gao A, et al. Epigenetic reprogramming of H3K27me3 and DNA methylation during leaf-to-callus transition in peach. Horticulture Research. 2022

Lin B, Lu B, Hsieh I, et al. Synergy of GSK-J4 With Doxorubicin in KRAS-Mutant Anaplastic Thyroid Cancer. Frontiers in Pharmacology. 2020, 11

Chu X, et al. GSK-J4 induces cell cycle arrest and apoptosis via ER stress and the synergism between GSK-J4 and decitabine in acute myeloid leukemia KG-1a cells. Cancer Cell Int. 2020 Jun 3;20:209.

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Chen, Hong, et al. . Histone demethylase UTX is a therapeutic target for diabetic kidney disease [J]. J Physiol. 2019 Mar;597(6):1643-1660.

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