GSK-J4

Cat. No.: HY-15648B

CAS No.: 1373423-53-0

Molecular Formula: $C_{24}H_{27}N_5O_2$

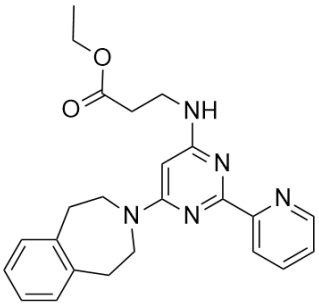
Molecular Weight: 417.5

Target: Histone Demethylase; Apoptosis

Pathway: Epigenetics; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 36 mg/mL (86.23 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3952 mL	11.9760 mL	23.9521 mL
5 mM	0.4790 mL	2.3952 mL	4.7904 mL
10 mM	0.2395 mL	1.1976 mL	2.3952 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.98 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.98 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.98 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK-J4 is a potent dual inhibitor of H3K27me3/me2-demethylases JMJD3/KDM6B and UTX/KDM6A with IC_{50}s of 8.6 and 6.6 μM, respectively. GSK-J4 inhibits LPS-induced TNF-α production in human primary macrophages with an IC_{50} of 9 μM. GSK J4 is a cell permeable prodrug of GSK-J1[1][2][3]. GSK-J4 induces endoplasmic reticulum stress-related apoptosis[4].

IC_{50} & Target

IC50: 8.6 μM (JMJD3/KDM6B), 6.6 μM (UTX/KDM6A)[6]

In Vitro

GSK-J4 has cellular activity in Flag-JMJD3-transfected HeLa cells, in which GSK-J4 prevents the JMJD3-induced loss of nuclear H3K27me3 immunostaining. Administration of GSK-J4 increases total nuclear H3K27me3 levels in untransfected cells. GSK-J4 significantly reduces the expression of 16 of 34 LPS-driven cytokines, including tumour-necrosis factor-α (TNF-α)[1].

GSK-J4 (5 μM; 48 hours) causes a more than 3-fold increase in mouse podocyte H3K27me3 content. H3K27me3 levels in cultured podocytes, GSK-J4 reduces Jagged-1 mRNA and Jagged-1 protein levels. Correspondingly, when exposed podocytes to the inducer of dedifferentiation TGF-β1, pretreatment with GSK-J4 preventes both the increase in intracellular N1-ICD levels and the increase in α-SMA and the decrease in podocin mRNA levels[2].

GSK-J4 (10, 25 nM) acts upon DCs promoting the differentiation of Treg cells, improving Treg stability and suppressive capacities, without affecting the differentiation of Th1 and Th17 cells[3].

GSK-J4 inhibits JMJD3 expression that is induced by TGF-β1[4].

GSK-J4 inhibits H3K4 demethylation at Xist, Nodal, and HoxC13 in female embryonic stem cells[5].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

GSK-J4 Hydrochloride (10 mg/kg; i.p.; thrice-weekly for 10 weeks) attenuates the development of kidney disease in diabetic mice[2].

GSK-J4 (0.5 mg/kg, i.p.) significantly reduces the severity and delays the onset of the disease of the mouse model of experimental autoimmune encephalomyelitis[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Eight-week-old male db/m and db/db mice[2]
Dosage:	10 mg/kg
Administration:	i.p.; thrice-weekly for 10 weeks
Result:	Attenuated the development of kidney disease in diabetic mice.

CUSTOMER VALIDATION

- Sci Adv. 2021 Mar 5;7(10):eabe7853.
- J Clin Invest. 2018 Jan 2;128(1):483-499.
- Biochim Biophys Acta Mol Cell Biol Lipids. 2021 Feb 8;158901.
- Cancer Cell Int. 2020 Jun 3;20:209.
- Biochem J. 2019 Jun 26;476(12):1741-1751.

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REFERENCES

[1]. Kruidenier L, et al. A selective jumonji H3K27 demethylase inhibitor modulates the proinflammatory macrophage response. Nature. 2012 Aug 16;488(7411):404-8.

[2]. Donas C, et al. The histone demethylase inhibitor GSK-J4 limits inflammation through the induction of a tolerogenic phenotype on DCs. J Autoimmun. 2016 Dec;75:105-117.

[3]. Yapp C, et al. H3K27me3 demethylases regulate in vitro chondrogenesis and chondrocyte activity in osteoarthritis. Arthritis Res Ther. 2016 Jul 7;18(1):158

[4]. Kamikawa YF, et al. Histone demethylation maintains Prdm14 and Tsix expression and represses xIst in embryonic stem cells. PLoS One. 2015 May 20;10(5):e0125626

[5]. Heinemann B, et al. Inhibition of demethylases by GSK-J1/J4. Nature. 2014 Oct 2;514(7520):E1-2

[6]. Majumder S, et al. Shifts in podocyte histone H3K27me3 regulate mouse and human glomerular disease. J Clin Invest. 2018 Jan 2;128(1):483-499.

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