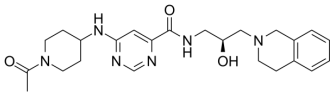
GSK3326595

Cat. No.:	HY-101563
CAS No.:	1616392-22-3
Molecular Formula:	$C_{24}H_{32}N_6O_3$
Molecular Weight:	452.55
Target:	Histone Methyltransferase; SARS-CoV; MDM-2/p53; CDK; Apoptosis
Pathway:	Epigenetics; Anti-infection; Apoptosis; Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 62.5 mg/mL (138.11 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2097 mL	11.0485 mL	22.0970 mL
	5 mM	0.4419 mL	2.2097 mL	4.4194 mL
	10 mM	0.2210 mL	1.1049 mL	2.2097 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.52 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.52 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.08 mg/mL (4.60 mM); Clear solution; Need ultrasonic
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.60 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.60 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK3326595 is a protein arginine methyltransferase 5 (PRMT5) inhibitor. GSK3326595 decreases SARS-CoV-2 infection, inhibits cancer cell proliferation and induces pro-inflammatory macrophage polarization and increases hepatic triglyceride levels without affecting atherosclerosis. GSK3326595 can be used for research of relapsed/refractory mantle cell lymphoma

	[1][2][3][4][5].

IC_{50} & Target	PRMT5	CDK4	CDK6

In Vitro

GSK3326595 (10-100 nM, 24-72 h) inhibits SARS-CoV-2spike pseudovirus infection HEK-293 cells and A549 cells by attenuating ACE2-RBD interaction[1].
GSK3326595 (100 nM, 12 h) primes peritoneal macrophages to IFN-gamma-induced M1 polarization[3].
GSK3326595 (0.15-10 μM, 72 h) induces cell death in MCL cell[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[4]

Cell Line:	HEK-293T cells, A549 cells
Concentration:	10 nM, 25 nM, 50 nM, 100 nM
Incubation Time:	48 h
Result:	Strongly inhibited ACE2-RBD interaction at low concentration. Inhibited SARS-CoV-2 Omicron and other variants Spike1 binding with ACE2. Inhibits SARS-CoV-2 spike pseudovirus infection host cells.

Cell Cytotoxicity Assay[1]

Cell Line:	MCL cells
Concentration:	0.15 μM, 0.3 μM, 0.6 μM, 1.25 μM, 2.5 μM, 5 μM, 10 μM
Incubation Time:	72 h
Result:	Resulted in modest growth inhibition in MCL cells.

In Vivo

GSK3326595 (5 mg/kg, Intraperitoneal injection, three times a week for 9 weeks) increased hepatic triglyceride levels without affecting atherosclerosis in LDL receptor knockout mice[3].GSK3326595 (25-50 mg/kg, Oral, once a day for 2 weeks) enhances the efficacy of anti-programed cell death protein 1 (PD-1) immune checkpoint therapy (ICT) in hepatocellular carcinoma (HCC) in myelocytomatosis transgene turned on (MYC-ON) mice[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	LDL receptor knockout mice[3]
Dosage:	5 mg/kg
Administration:	Intraperitoneal injection (i.p.)
Result:	Did not alter atherosclerosis susceptibility. Increased hepatic triglyceride levels without changing the hyperlipidemia extent. Activated genes involved in fatty acid acquisition.

Animal Model:	myelocytomatosis transgene turned on mice[5]
Dosage:	25 mg/kg, 50 mg/kg
Administration:	Oral
Result:	Significantly suppressed tumor growth at 50 mg/kg. Showed better therapeutic efficacy at 25 mg/kg.

CUSTOMER VALIDATION

- Nat Commun. 2021 Jun 8;12(1):3444.
- J Exp Clin Cancer Res. 2022 Oct 5;41(1):293.
- EMBO Mol Med. 2023 Jul 17;e17248.
- Cell Mol Life Sci. 2023 Jan 17;80(2):43.
- Oncogene. 2021 Apr;40(15):2711-2724.

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REFERENCES

[1]. Li Z, et al. GSK3326595 is a promising drug to prevent SARS-CoV-2 Omicron and other variants infection by inhibiting ACE2-R671 di-methylation [J]. Journal of Medical Virology, 2023, 95(1): e28158.

[2]. Fedoriw A, et al. Anti-tumor activity of the type I PRMT inhibitor, GSK3368715, synergizes with PRMT5 inhibition through MTAP loss [J]. Cancer cell, 2019, 36(1): 100-114. e25.

[3]. Zhang Y, et al. PRMT5 inhibition induces pro-inflammatory macrophage polarization and increased hepatic triglyceride levels without affecting atherosclerosis in mice [J]. Journal of Cellular and Molecular Medicine, 2023, 27(8): 1056-1068.

[4]. Che Y, et al. Exploiting PRMT5 as a target for combination therapy in mantle cell lymphoma characterized by frequent ATM and TP53 mutations [J]. Blood cancer journal, 2023, 13(1): 27.

[5]. Luo Y, et al. Myelocytomatosis-protein arginine N-methyltransferase 5 Axis defines the tumorigenesis and immune response in hepatocellular carcinoma [J]. Hepatology, 2021, 74(4): 1932-1951.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA