GSK 3 Inhibitor IX

Cat. No.: HY-10580

CAS No.: 667463-62-9

Molecular Formula: $C_{16}H_{10}BrN_3O_2$

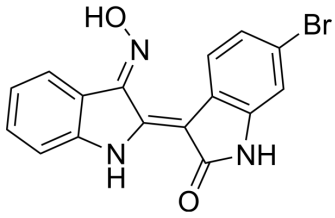
Molecular Weight: 356.17

Target: GSK-3; CDK; Apoptosis

Pathway: PI3K/Akt/mTOR; Stem Cell/Wnt; Cell Cycle/DNA Damage; Apoptosis

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 23 mg/mL (64.58 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.8076 mL	14.0382 mL	28.0765 mL
5 mM	0.5615 mL	2.8076 mL	5.6153 mL
10 mM	0.2808 mL	1.4038 mL	2.8076 mL

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

BIOLOGICAL ACTIVITY

Description

GSK 3 Inhibitor IX (6-Bromoindirubin-3'-oxime; BIO) is a potent, selective, reversible and ATP-competitive inhibitor of GSK-3 α/β and CDK1-cyclinB complex with IC_{50}s of 5 nM/320 nM/80 nM for (GSK-3α/β)/CDK1/CDK5, respectively.

IC_{50} & Target

GSK-3α 5 nM (IC_{50})	GSK-3β 5 nM (IC_{50})	CDK5/p35 80 nM (IC_{50})	Cdk1/cyclin B 320 nM (IC_{50})
cdk2/cyclin A 300 nM (IC_{50})	Cdk4/cyclin D1 10 μM (IC_{50})	MAPKK 10 μM (IC_{50})	protein kinase Cα 12 μM (IC_{50})

In Vitro

GSK 3 Inhibitor IX (BIO) is a specific inhibitor of glycogen synthase kinase-3 (GSK-3), with IC_{50} of 5 nM for GSK-3α/β, shows > 16-fold selectivity over CDK5.

GSK 3 Inhibitor IX interacts within the ATP binding pocket of these kinases, reduces β-catenin phosphorylation on a GSK-3-specific site in cellular models, closely mimicks Wnt signaling in Xenopus embryos[1].

In human and mouse embryonic stem cells, GSK 3 Inhibitor IX (BIO) maintains the undifferentiated phenotype and sustains

	expression of the pluripotent state-specific transcription factors Oct-3/4, Rex-1 and Nanog. GSK 3 Inhibitor IX (BIO)-mediated Wnt activation is functionally reversible, as withdrawal of the compound leads to normal multidifferentiation programs in both human and mouse embryonic stem cells[2]. GSK 3 Inhibitor IX (BIO) promotes proliferation in mammalian cardiomyocytes[3]. GSK 3 Inhibitor IX (BIO) is also a pan-JAK inhibitor, with IC_{50} values of 0.03, 1.5, 8.0, 0.5 μM for TYK2, JAK1, JAK2 and JAK3, respectively. GSK 3 Inhibitor IX (BIO) selectively inhibits phosphorylation of STAT3 and induces apoptosis of human melanoma cells[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GSK 3 Inhibitor IX (BIO) (50 mg/kg, p.o.) suppresses melanoma tumor growth in a mouse xenograft model[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	COS1, Hepa (wild-type, CEM/LM AhR deficient and ELB1 ARNT deficient), or SH-SY5Y cells are grown in 6 cm culture dishes in Dulbecco's Modified Medium (DMEM) containing 10% fetal bovine serum. For treatment, IO (5 μM), GSK 3 Inhibitor IX (BIO) (5 or 10 μM), MeBIO (5 or 50 μM), LiCl (20 or 40 mM), or mock solution (DMSO, 0.5% final concentration) is added to medium when cell density reaches appr 70% confluence. After 12 (SH-SY5Y) or 24 hours, the cells, while still in plate, are lysed with lysis buffer (1% SDS, 1 mM sodium orthovanadate, 10 mM Tris [pH 7.4]). The lysate is passed several times through a 26G needle, centrifuged at 10,000× g for 5 min, and adjusted to equal protein concentration. About 8 μg of each sample is loaded for immunoblotting. Enhanced chemiluminescence is used for detection. The following primary antibodies are used: mouse anti-β-catenin CT, mouse anti-phospho-β-catenin, mouse anti-GSK-3 β, mouse anti-GSK-3 phosphoTyr216, rabbit anti-AhR (Aryl hydrocarbon receptor), and rabbit anti-actin. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	BALB/c mice (at 6-8 weeks old) and immunodeficient NOD/SCID/IL2Rgamma null (NSG) mice (female at 6-8 weeks old) are used in the assay. A2058 human melanoma cells at 5×10^6 cells in serum free medium are inoculated subcutaneously into the dorsal area of NSG mice to create xenograft model. When tumors become palpable, 6 GSK 3 Inhibitor IX (BIO) or vehicle control is administered via oral gavage once daily at 50 mg/kg body weight. Tumor growth is monitored every other day. Tumor volumes are measured every 3 to 4 days. Tumor volumes are calculated using the formula: 0.5 × (larger diameter) × (small diameter)^2. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Res. 2022 Jun;32(6):513-529.
- Chem Eng J. 19 November 2021, 133671.
- Cell Death Differ. 2020 Mar;27(3):1119-1133.
- Cell Rep. 2020 Jan 14;30(2):497-509.e4.
- J Transl Med. 2022 Oct 2;20(1):444.

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REFERENCES

[1]. Meijer L, et al. GSK-3-selective inhibitors derived from Tyrian purple indirubins. Chem Biol. 2003 Dec;10(12):1255-66.

[2]. Sato N, et al. Maintenance of pluripotency in human and mouse embryonic stem cells through activation of Wnt signaling by a pharmacological GSK-3-specific

inhibitor. Nat Med. 2004 Jan;10(1):55-63. Epub 2003 Dec 21.

[3]. Tseng AS, et al. The GSK-3 inhibitor BIO promotes proliferation in mammalian cardiomyocytes. Chem Biol. 2006 Sep;13(9):957-63.

[4]. Liu L1, et al. 6-Bromoindirubin-3'-oxime inhibits JAK/STAT3 signaling and induces apoptosis of human melanoma cells. Cancer Res. 2011 Jun 1;71(11):3972-9

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