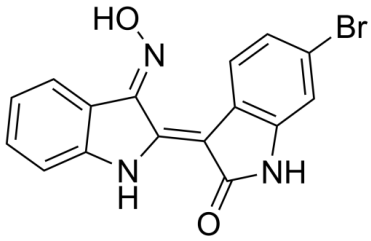
Data Sheet

Product Name:	GSK 3 Inhibitor IX
Cat. No.:	CS-3360
CAS No.:	667463-62-9
Molecular Formula:	$C_{16}H_{10}BrN_3O_2$
Molecular Weight:	356.17
Target:	Apoptosis; CDK; GSK-3
Pathway:	Apoptosis; Cell Cycle/DNA Damage; PI3K/Akt/mTOR; Stem Cell/Wnt
Solubility:	DMSO : ≥ 23 mg/mL



BIOLOGICAL ACTIVITY:

GSK 3 Inhibitor IX (6-Bromoindirubin-3'-oxime; BIO) is a potent, selective, reversible and ATP-competitive inhibitor of **GSK-3α/β** and **CDK1-cyclinB** complex with **IC_{50}**s of 5 nM/320 nM/80 nM for (GSK-3α/β)/CDK1/CDK5, respectively. IC50 & Target: IC50: 5 nM (GSK-3α/β), 320 nM (CDK1), 80 nM (CDK5)[1] ***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]. ***In Vivo:*** GSK 3 Inhibitor IX (BIO) (50 mg/kg, p.o.) suppresses melanoma tumor growth in a mouse xenograft model[4].

PROTOCOL (Extracted from published papers and Only for reference)

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. **Animal Administration:** BIO is freshly prepared in 30% Solutol as 10 mg/mL.[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.

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

CAIndexNames:

2H-Indol-2-one, 6-bromo-3-[(3E)-1,3-dihydro-3-(hydroxyimino)-2H-indol-2-ylidene]-1,3-dihydro-, (3Z)-

SMILES:

O/N=C(C1=CC=CC=C1N2)/C2=C3C(NC4=C/3C=CC(Br)=C4)=O

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