BIX-01294

Cat. No.: HY-10587
CAS No.: 935693-62-2
Molecular Formula: C_{28}H_{38}N_{6}O_{2}
Molecular Weight: 490.64
Target: Histone Methyltransferase; Autophagy
Pathway: Epigenetics; Autophagy
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: ≥ 110 mg/mL (224.20 mM)
H_{2}O: 1 mg/mL (2.04 mM; Need ultrasonic)
* "≥" means soluble, but saturation unknown.

Preparation of Stock Solutions

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td></td>
<td>2.0382 mL</td>
<td>10.1908 mL</td>
<td>20.3815 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.4076 mL</td>
<td>2.0382 mL</td>
<td>4.0763 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.2038 mL</td>
<td>1.0191 mL</td>
<td>2.0382 mL</td>
</tr>
</tbody>
</table>

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: ≥ 2.75 mg/mL (5.60 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.75 mg/mL (5.60 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.75 mg/mL (5.60 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
BIX-01294 is a reversible and highly selective G9a and GLP Histone Methyltransferase inhibitor, with IC_{50}s of 1.7 μM and 0.9 μM, respectively. BIX-01294 inhibits G9a/GLP by competing for binding with the amino acids N-terminal of the substrate lysine residue. BIX-01294, a (1H-1,4-diazepin-1-yl)-quinazolin-4-yl amine derivative, induces necroptosis and autophagy. BIX-01294 has antitumor activity in recurrent tumor cells.[1][2][3][4][5]
IC₅₀ & Target

| EHMT2/G9a/KMT1C | EHMT1/GLP/KMT1D |

In Vitro

BIX-01294 (2 μM; 48 h) selectively inhibits recurrent tumor cell growth[1].

?BIX-01294 (1 μM) leads to a marked increase in phosphorylation of S345 of MLKL[1].

?BIX-01294 (1 μM) significantly upregulates the canonical p53 targets Cdkn1a (p21) and Gadd45a in recurrent tumor cell lines [1].

?BIX-01294 (1 μM; 6 days) causes the reduction in H3K9me2 levels in primary and recurrent tumor cells[1].

?BIX-01294 leads to necroptotic cell death in recurrent tumor cells. Necrostatin-1 (30 μM) partially reverses cell death induced by BIX-01294 (750 nM; 24 h)[1].

?BIX-01294 (4.1 μM; for 2 days) causes around a 20% reduction, concomitant with a comparable increase in the unmodified H3K9 fragment in H3K9me2 in mouse ES cells. BIX-01294 causes pronounced reduction in H3K9me2 and a small decrease for H3K9me3 and H3K9me1 in wild-type ES cells[2].

?BIX-01294 has no inhibition of the other histone methyltransferases even at concentrations of 45 μM. BIX-01294 does not affect SUV39H1 (H320R) and PRMT1 within the tested concentration range (up to 10 μM)[2].

?BIX-01294 inhibits G9a in an uncompetitive manner with S-adenosyl-methionine (SAM)[2].

?BIX-01294 (1 μg/mL) causes reduction in the BrdU incorporation of fetal PASMCs. BIX-01294 treatment decreases the PASMCs migration induced by PDGF[3].

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

Cell Viability Assay[1]

| Cell Line: | Primary or recurrent tumor cells |
| Concentration: | 2 μM |
| Incubation Time: | 48 hours |
| Result: | Selectively inhibited recurrent tumor cell growth. |

In Vivo

BIX-01294 (10 mg/kg; IP; three times a week for 2 weeks) significantly reduces tumor growth and tumor burden in recurrent tumor cells. Primary tumor growth is not inhibited[1].

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

| Animal Model: | Female MMTV-rtTA;TetO-Her2/neu (MTB;TAN) and TetO-Her2/neu (TAN) mice with recurrent or primary tumor cells[2] |
| Dosage: | 10 mg/kg |
| Administration: | IP; three times a week for 2 weeks |
| Result: | Significantly reduced tumor growth and tumor burden in recurrent tumor cells. Primary tumor growth was not inhibited. Slowed the growth of orthotopic recurrent tumors in athymic nude recipients. |

CUSTOMER VALIDATION

- ACS Nano. 2023 Jan 19.
REFERENCES


Caution: Product has not been fully validated for medical applications. For research use only.

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