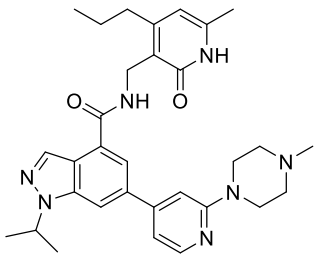
Product data sheet

MedKoo Cat#: 406270 Name: GSK343 CAS#: 1346704-33-3 Chemical Formula: $C_{31}H_{39}N_7O_2$ Exact Mass: 541.31652 Molecular Weight: 541.69	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

GSK343 is a potent, selective inhibitor of EZH2 with cellular activity. GSK343 inhibits EZH2 with an IC50 of 4nM and is over 1000-fold selective for other HMTs except EZH1 (60-fold selectivity). GSK343 inhibits H3K27 methylation in HCC1806 cells with an IC50 of <200nM as measured by immunofluorescence. GSK343 exhibited limited effects on the growth of EOC cells in conventional two-dimensional (2D) culture. In contrast, GSK343 significantly suppressed the growth of EOC cells cultured in 3D matrigel extracellular matrix (ECM), which more closely mimics the tumor microenvironment in vivo. Notably, GSK343 induces apoptosis of EOC cells in 3D but not 2D culture. In addition, GSK343 significantly inhibited the invasion of EOC cells.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	31.86	58.82
Ethanol	7.0	12.92
DMF	25.0	46.15
DMF:PBS (pH 7.2) (1:1)	0.5	0.92

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.85 mL	9.23 mL	18.46 mL
5 mM	0.37 mL	1.85 mL	3.69 mL
10 mM	0.18 mL	0.92 mL	1.85 mL
50 mM	0.04 mL	0.18 mL	0.37 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Yang PM, Hong YH, Hsu KC, Liu TP. p38α/S1P/SREBP2 activation by the SAM-competitive EZH2 inhibitor GSK343 limits its anticancer activity but creates a druggable vulnerability in hepatocellular carcinoma. Am J Cancer Res. 2019 Oct 1;9(10):2120-2139. PMID: 31720078; PMCID: PMC6834481.
2. Xiong X, Zhang J, Li A, Dai L, Qin S, Wang P, Liu W, Zhang Z, Li X, Liu Z. GSK343 induces programmed cell death through the inhibition of EZH2 and FBP1 in osteosarcoma cells. Cancer Biol Ther. 2020;21(3):213-222. doi: 10.1080/15384047.2019.1680061. Epub 2019 Oct 25. PMID: 31651209; PMCID: PMC7012145.

In vivo study

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1. Yue D, Wang Z, Yang Y, Hu Z, Luo G, Wang F. EZH2 inhibitor GSK343 inhibits sepsis-induced intestinal disorders. Exp Ther Med. 2021 May;21(5):437. doi: 10.3892/etm.2021.9854. Epub 2021 Feb 26. PMID: 33747174; PMCID: PMC7967880.
2. Bownes LV, Williams AP, Marayati R, Stafman LL, Markert H, Quinn CH, Wadhwani N, Aye JM, Stewart JE, Yoon KJ, Mroczek-Musulman E, Beierle EA. EZH2 inhibition decreases neuroblastoma proliferation and in vivo tumor growth. PLoS One. 2021 Mar 9;16(3):e0246244. doi: 10.1371/journal.pone.0246244. PMID: 33690617; PMCID: PMC7942994.

7. Bioactivity

Biological target:

GSK343 is an EZH2 inhibitor with an IC50 of 4 nM.

In vitro activity

As shown in Figure 2A, GSK343 increased the level of mature SREBP2, but not SREBP1, in both HepG2 and PLC5 cells. Although the expression of SREBP1 precursor in PLC5 cells was reduced by GSK343, no increase of mature SREBP1 was observed. To confirm the activation of SREBP2, the nuclear localization and DNA binding activity of SREBP1/2 were examined. Consistently, GSK343 increased nuclear level and DNA binding ability of SREBP2, but not SREBP1, in HepG2 and PLC5 cells (Figure 2B and 2C).

Reference: Am J Cancer Res. 2019; 9(10): 2120–2139. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6834481/

In vivo activity

GSK343, which is an EZH2 inhibitor, was used to treat CLP mice to observe whether inhibition of EZH2 could protect the intestine against sepsis-induced injury. At the end of the experiment, animals were sacrificed and H&E staining was performed on small intestinal tissue sections. Fig. 2A demonstrates the results of H&E staining in the intestinal tissues of mice in different groups. The ileum tissue structure of the mice in the sham operation group was normal, the intestinal villi were arranged neatly and the villi structure was clear. In the CLP group, however, evident edema, hyperemia, necrosis and inflammatory cell infiltration were observed, accompanied by missing apical epithelial cells of the villi and thinner and shorter microvilli. Compared with the CLP group, the intestinal structure of the mice in the GSK343 treatment group was relatively normal, with relieved intestinal villi edema and inflammation. The levels of inflammatory cytokines, including TNF-α, IL-1β and IL-6, in the serum and intestinal tissues of mice in different groups are presented in Fig. 2B and C. It was indicated that CLP stimulation significantly promoted the production of all inflammatory cytokines, and this increase was reversed by GSK343 treatment.

Reference: Exp Ther Med. 2021 May; 21(5): 437. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7967880/