

Product Data Sheet

Product Name: GW5074

Cat. No.: GC11685

Chemical Properties

Cas. No. 220904-83-6

Chemical Name (3Z)-3-[(3,5-dibromo-4-hydroxyphenyl)methylidene]-5-iodo-1H-indol-2-one

SMILES C1=CC2=C(C=C1I)C(=CC3=CC(=C(C(=C3)Br)O)Br)C(=O)N2

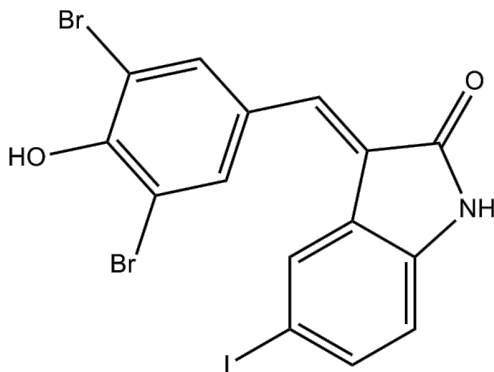
Formula C15H8Br2INO2 M.Wt 520.95

Solubility >26.1mg/mL in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines HCT116 cells (human colorectal cancer cell line), LDHB-knockout HCT116 cells stably expressing HA-LDHBWT or HA-LDHBK329Q

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Preparation Method HCT116 cells and derived lines were maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum (FBS) at 37°C, 5% CO₂. For GW5074 treatment, HCT116 cells were transiently transfected with HA-LDHBWT for 48h, or LDHB-KO HCT116 cells were transfected with HA-LDHBWT/HA-LDHBK329Q for 48h, followed by GW5074 treatment at 100μM for the last 24h.

Reaction Conditions 100μM; 24h

Applications GW5074 reduced SIRT5 protein level, increased LDHB acetylation at K329, and inhibited LDHB enzymatic activity in HCT116 cells. GW5074 also downregulated autophagic flux and induced apoptosis in HCT116 cells. When SIRT5 was inhibited by GW5074, LDHB-KO HCT116 cells expressing HA-LDHBWT and those expressing HA-LDHBK329Q showed comparable levels of autophagy and apoptosis.

Animal experiment [2]:

Animal models Six-week-old male ICR mice

Preparation Method Mice were exposed to sidestream smoke from four commercial filter cigarettes (1.0mg nicotine; 12mg tar) daily, 6 days/week for 4 weeks. After the first week of smoke exposure, mice in GW5074 groups received intraperitoneal injection of GW5074 every day for 3 weeks, while sham control received equal volume of saline. 24h after the last smoke exposure, mice were sacrificed for tracheal ring segment myograph test and tracheal histopathology analysis.

Dosage form 0.5mg/kg and 2mg/kg; i.p.; daily for 3 weeks

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Applications

Sidestream smoke exposure significantly enhanced mouse airway contractile responses to carbachol, endothelin-1 and potassium. GW5074 suppressed the smoke-induced airway contractile hyperresponsiveness in a dose-dependent manner, attenuated tracheal inflammatory cell infiltration and mucous gland hypertrophy, while airway epithelium-dependent relaxation was not affected.

References:

- [1] Shi L, Yan H, An S, et al. SIRT5-mediated deacetylation of LDHB promotes autophagy and tumorigenesis in colorectal cancer. *Mol Oncol.* 2019 Feb;13(2):358-375.
- [2] Li S, Liu J, Tan J, et al. Inhibition of Raf1 ameliorates bleomycin-induced pulmonary fibrosis through attenuation of TGF- β 1 signaling. *Am J Physiol Lung Cell Mol Physiol.* 2018 Aug 1;315(2):L241-L247.

Background

GW5074 is a potent and selective c-Raf inhibitor ($IC_{50}=9nM$). GW5074 disrupts cell proliferation and viral replication by inhibiting c-Raf activity and blocking the Ras/Raf/MEK/ERK (MAPK) cascade, while exerting MEK-ERK and Akt-independent neuroprotective effects through Ras/NF- κ B-related signaling. GW5074 can be used in research related to tumors, neurodegenerative diseases, and JC polyomavirus (JCPyV) infection^[1-4].

In vitro, GW5074 (100 μ M) treated HCT116 cells and LDHB-knockout HCT116 cells stably expressing HA-LDHBWT/HA-LDHBK329Q for 24h. GW5074 reduced SIRT5 protein levels, increased LDHB acetylation at Lys329, inhibited LDHB enzymatic activity, downregulated autophagy, and induced apoptosis^[5]. GW5074 (2 μ M) combined with all-trans retinoic acid (1 μ M) treated t(15;17)-negative human myeloblastic leukemia HL-60 cells and two retinoic acid-resistant sublines R38⁺ and R38⁻ for 48h. GW5074 combined with all-trans retinoic acid enhanced CD11b expression and G1/G0 cell cycle arrest in parental HL-60 cells. In R38⁻ cells, GW5074 upregulated all-trans retinoic acid-induced CD38 expression. In R38⁺ cells, GW5074 upregulated all-trans retinoic acid-induced CD11b expression and rescued G1/G0 arrest in both resistant cell lines^[6].

In vivo, GW5074 (2mg/kg) was intraperitoneally injected into bleomycin (2U/kg; single intranasal instillation)-induced pulmonary fibrosis model C57BL/6 mice, once every 2 days for a total of 7

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injections. GW5074 reduced fibronectin expression in mouse lung tissue, decreased collagen deposition and inflammatory cell infiltration, lowered the Ashcroft score for pulmonary fibrosis, and alleviated bleomycin-induced pulmonary fibrosis^[7]. GW5074 (0.5mg/kg or 2mg/kg; daily) was intraperitoneally injected into ICR mice exposed to sidestream smoke for 4 weeks (drug administration started after the first week of smoke exposure and lasted for 3 weeks). GW5074 significantly inhibited sidestream smoke-induced airway contractile hyperresponsiveness to carbachol, endothelin-1, and potassium, and attenuated tracheal inflammatory cell infiltration and mucous gland hypertrophy^[8].

References:

- [1] Chen J, Yu Q, Patterson E, et al. Dinitroaniline Herbicide Resistance and Mechanisms in Weeds. *Front Plant Sci.* 2021 Mar 25;12:634018.
- [2] Singh B, Yun S, Gil Y, et al. The Role of Colchicine in Plant Breeding. *Int J Mol Sci.* 2025 Jul 14;26(14):6743.
- [3] Basit A, Lim KB. Systematic approach of polyploidy as an evolutionary genetic and genomic phenomenon in horticultural crops. *Plant Sci.* 2024 Nov;348:112236.
- [4] Gantait S, Mukherjee E. Induced autopolyploidy-a promising approach for enhanced biosynthesis of plant secondary metabolites: an insight. *J Genet Eng Biotechnol.* 2021 Jan 8;19(1):4.
- [5] Shi L, Yan H, An S, et al. SIRT5-mediated deacetylation of LDHB promotes autophagy and tumorigenesis in colorectal cancer. *Mol Oncol.* 2019 Feb;13(2):358-375.
- [6] Jensen HA, Bunaciu RP, Varner JD, et al. GW5074 and PP2 kinase inhibitors implicate nontraditional c-Raf and Lyn function as drivers of retinoic acid-induced maturation. *Cell Signal.* 2015 Aug;27(8):1666-75.
- [7] Li S, Liu J, Tan J, et al. Inhibition of Raf1 ameliorates bleomycin-induced pulmonary fibrosis through attenuation of TGF- β 1 signaling. *Am J Physiol Lung Cell Mol Physiol.* 2018 Aug 1;315(2):L241-L247.
- [8] Lei Y, Cao YX, Xu CB, et al. The Raf-1 inhibitor GW5074 and dexamethasone suppress sidestream smoke-induced airway hyperresponsiveness in mice. *Respir Res.* 2008 Nov 3;9(1):71.

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