

Product Data Sheet

Product Name: PD 146176

Cat. No.: GC12205

Chemical Properties

Cas. No. 4079-26-9

Chemical Name 6,11-dihydrothiochromeno[4,3-b]indole

SMILES C12=C(C3=CC=CC=C3SC2)NC4=CC=CC=C14

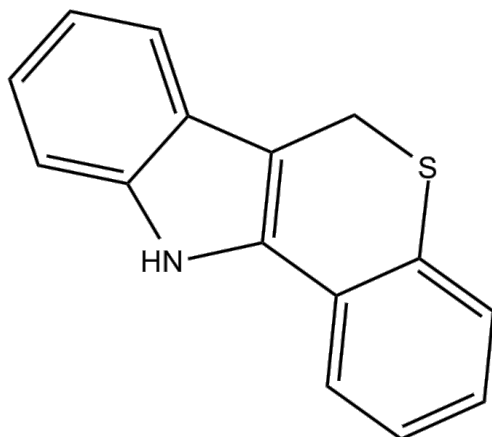
Formula $C_{15}H_{11}NS$ M.Wt 237.32

Solubility DMF: 10 mg/ml, DMF:PBS (pH 7.2) (1:5): 0.15 mg/ml, DMSO: 10 mg/ml, Ethanol: 2 mg/ml
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]:

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

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Cell lines murine melanoma cell line B16F10

Preparation Method 1 × 10⁴ cells per well were seeded in each well of a 96-well tissue culture plate and left overnight in the incubator. The cells were incubated with PD 146176 for 24, 48, or 72 h similar to the MTT assay.

Reaction Conditions 0.5, 1, 2, 10, 20, 40 μM for 24, 48, 72 hours

Applications PD 146176 induced cell cycle arrest in G1 phase at 8 h with decrease of cells in S and G2/M phase. The effect on cell morphology is visible observed after 16 h with cells becoming smaller and rounded.

Animal experiment [2]:

Animal models C57BL/6 mice

Preparation Method One group was untreated and ate ground rodent chow for 7 days while the experimental group was fed ground rodent chow with the selective PD 146176 added at a concentration to achieve a dose of about 400 mg/kg/day

Dosage form Fed with diet, 400 mg/kg/day, 7 days

Applications The mice that were fed PD 146176 lost significantly more weight at 3-5 days after starting dextran sodium sulfate, compared to the corresponding day for the control mice.

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References:

- [1]: Da-Costa-Rocha I, Prieto J M. In vitro effects of selective COX and LOX inhibitors and their combinations with antineoplastic drugs in the mouse melanoma cell line B16F10[J]. International journal of molecular sciences, 2021, 22(12): 6498.
- [2]: Joshi Y B, Giannopoulos P F, Praticò D. The 12/15-lipoxygenase as an emerging therapeutic target for Alzheimer's disease[J]. Trends in pharmacological sciences, 2015, 36(3): 181-186.

Background

PD 146176 is one of the potent and selective inhibitors of reticulocyte 15-LOX-1 [1]. PD 146176 inhibited the activity of h-15-LOX-1 with IC₅₀ value of $16 \pm 2.5 \mu\text{M}$, and K_i value of $3.9 \pm 0.6 \mu\text{M}$ [2].

PD 146176 (1 $\mu\text{g ml}^{-1}$) inhibited the induction of both arginase-1 and mannose receptor mRNA in both rIL-4-treated and RSV-infected WT macrophages, whereas enhancing the induction of COX-2 mRNA [3]. PD 146176 suggested that it causes strong cell cycle arrest in G1 phase. PD 146176 at its IC₅₀, did not show any inhibitory effect on cell directional migration but greatly increased the activity of the caspases in B16F10 cells [4]. PD 146176 significantly prevented glutamate-induced cell death in a concentration-dependent manner. PD 146176 fully protected HT-22 cells against glutamate toxicity at a concentration of 0.5 μM and significantly reduced the annexin-V/propidium iodide-positive cells [5].

PD 146176 treated 3xTg mice had significant reductions in A β peptide levels, amyloid plaque burden, tau phosphorylation, and insoluble tau deposition in comparison with controls [6,7]. AD model mice in the control group showed a worsening of memory and learning abilities, whereas mice receiving PD 146176 were undistinguishable from wild-type mice [7].

References:

- [1]. Orafai A, Mousavian M, Orafai H, et al. An overview of lipoxygenase inhibitors with approach of in vivo studies[J]. Prostaglandins & Other Lipid Mediators, 2020, 148: 106411.
- [2]. Eleftheriadis N, Thee S, Te Biesebeek J, et al. Identification of 6-benzoyloxysalicylates as a novel class of inhibitors of 15-lipoxygenase-1[J]. European Journal of Medicinal Chemistry, 2015, 94: 265-275.

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- [3]. Shirey K A, Lai W, Pletneva L M, et al. Role of the lipoxygenase pathway in RSV-induced alternatively activated macrophages leading to resolution of lung pathology[J]. Mucosal immunology, 2014, 7(3): 549-557.
- [4]. Da-Costa-Rocha I, Prieto J M. In vitro effects of selective COX and LOX inhibitors and their combinations with antineoplastic drugs in the mouse melanoma cell line B16F10[J]. International journal of molecular sciences, 2021, 22(12): 6498.
- [5]. Tobaben S, Grohm J, Seiler A, et al. Bid-mediated mitochondrial damage is a key mechanism in glutamate-induced oxidative stress and AIF-dependent cell death in immortalized HT-22 hippocampal neurons[J]. Cell Death & Differentiation, 2011, 18(2): 282-292.
- [6]. Oddo S, Caccamo A, Shepherd J D, et al. Triple-transgenic model of Alzheimer's disease with plaques and tangles: intracellular A β and synaptic dysfunction[J]. Neuron, 2003, 39(3): 409-421.
- [7]. Di Meco A, Li J G, Blass B E, et al. 12/15-Lipoxygenase inhibition reverses cognitive impairment, brain amyloidosis, and tau pathology by stimulating autophagy in aged triple transgenic mice[J]. Biological psychiatry, 2017, 81(2): 92-100.

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