Pifithrin-α hydrobromide

Cat. No.: HY-15484

CAS No.: 63208-82-2

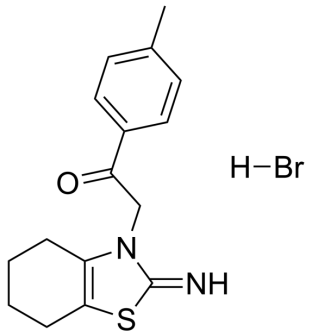
Molecular Formula: $C_{16}H_{19}BrN_2OS$

Molecular Weight: 367.3

Target: MDM-2/p53; Aryl Hydrocarbon Receptor; Ferroptosis; Apoptosis

Pathway: Apoptosis; Immunology/Inflammation

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (136.13 mM)
H_2O : 1.25 mg/mL (3.40 mM; Need ultrasonic)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7225 mL	13.6127 mL	27.2254 mL
5 mM	0.5445 mL	2.7225 mL	5.4451 mL
10 mM	0.2723 mL	1.3613 mL	2.7225 mL

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: ≥ 2.5 mg/mL (6.81 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.81 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Pifithrin-α hydrobromide is a p53 inhibitor which blocks its transcriptional activity and prevents cells from apoptosis. Pifithrin-α hydrobromide is also an aryl hydrocarbon receptor (AhR) agonist.

IC_{50} & Target

p53[1]
AhR[2]

In Vitro

Pifithrin-α (PFT-α) hydrobromideis a water-soluble compound that could suppress p53 protein transcription. Pifithrin-α can

	suppress glucose oxidase (GOX)-induced p53 protein increase in whole cell lysates, but cyclosporine A (CsA) fails to show such an inhibition effect. Notably, Pifithrin-α is able to block the GOX-induced Bcl-2 protein reduction. Similarly, it is Pifithrin-α rather than CsA that able to prevent the Bax increasing in whole cell lysates[1]. Pifithrin-α inhibits p53-dependent apoptosis through an undetermined mechanism. Pifithrin-α also acts as an aryl hydrocarbon receptor (AhR) agonist and. Pifithrin-α is a potent AhR agonist as determined by its ability to bind the AhR, induce formation of its DNA binding complex, activate reporter activity, and up-regulate the classic AhR target gene CYP1A1[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	When the experiment is performed with Pifthirin-α (PFT-α) hydrobromide, a pharmacological p53 inhibitor, the percentage of annexin V-positive Foxe3$^{-/-}$ SMCs decreases to WT levels. Pifithrin-α (2.2 mg/kg, i.p.) significantly reduces the incidence of aortic rupture and intramural hematomas in Foxe3$^{-/-}$ mice that underwent transverse aortic constriction (TAC) (50% to 17%, P<0.05). After Pifthirin-α treatment, the mean diameter of the ascending aorta and the percentage of TUNEL-positive cells in the aortic media are also normalized to WT levels in surviving Foxe3$^{-/-}$ animals (P<0.05)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	The ligand binding competition assays are performed. Cytosolic cell extracts from Hepa-1 cells are generated by the resuspension of the cell pellets in HEDG buffer [25 mM Hepes, 1 mM EDTA, 1 mM dithiothreitol, and 10% (v/v) glycerol, pH 7.5] containing 0.4 mM leupeptin, 4 mg/mL aprotinin, and 0.3 mM phenylmethylsulfonyl fluoride, homogenization, and centrifugation at 100,000 g for 45 min. Aliquots of the supernatant (120 μg) are incubated at room temperature for 2 h with the indicated concentrations of Pifithrin-α in the presence of 3 nM [^{3}H]TCDD in HEDG buffer. After incubation on ice with hydroxyapatite for 30 min, HEDG buffer with 0.5% Tween 80 is added. The samples are centrifuged, washed twice, resuspended in 0.2 mL of scintillation fluid, and subjected to scintillation counting. Nonspecific binding is determined using a 150-fold molar excess of TCDF and subtracted from the total binding to obtain the specific binding. The specific binding is reported relative to [^{3}H]TCDD alone[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	The human hepatoma cell lines HepG2 (p53++) are cultured in RMPI 1640 medium with 10% fetal bovine serum (FBS), and 1% penicillin/streptomycin at 37°C in an atmosphere containing 5% CO_2. Cells are exposed to GOX (0-5 0U) for 0-8 hours with or without Pifithrin-α (20 μM/L), Pifithrin-μ (5 μM/L), CsA (10 μM/L), Sanglifehrin A (20 μM/L) and NAC (5 mM/L) for 1 hour, respectively. After treatment, cells are collected and processed for further experiments[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] The Foxe3-null (Foxe3$^{-/-}$) mice are used. To investigate the role of p53 in Foxe3-related apoptosis, Pifithrin-α is administered by i.p. injection at a dosage of 2.2 mg/kg, then dissolved in PBS 1 hour before TAC and then every 48 hours. Animals are euthanized 2 weeks after the surgery, and the ascending aortic tissues are harvested for either RNA, total protein, histomorphometric analysis, or TUNEL assay. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- ACS Nano. 2023 Nov 8.
- J Hazard Mater. 2021 Mar 15;406:124316.
- EMBO J. 2022 Jan 5;e108946.
- Biomark Res. 2024 Jan 25;12(1):13.
- J Adv Res. 2024 Jan 12:S2090-1232(24)00025-0.

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REFERENCES

[1]. Yu W, et al. Cyclosporine A Suppressed Glucose Oxidase Induced P53 Mitochondrial Translocation and Hepatic Cell Apoptosis through Blocking Mitochondrial Permeability Transition. Int J Biol Sci. 2016 Jan 1;12(2):198-209.

[2]. Hoagland MS, et al. The p53 Inhibitor Pifithrin-α Is a Potent Agonist of the Aryl Hydrocarbon Receptor. J Pharmacol Exp Ther. 2005 Aug;314(2):603-10.

[3]. Kuang SQ, et al. FOXE3 mutations predispose to thoracic aortic aneurysms and dissections. J Clin Invest. 2016 Mar 1;126(3):948-61.

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