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# Pifithrin-α (hydrobromide)

## Catalog No: tcsc1010

### Available Sizes

**Size:** 5mg

**Size:** 10mg

**Size:** 25mg

**Size:** 50mg

### Specifications

**CAS No:**
63208-82-2

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

**Pathway:**
Apoptosis;Immunology/Inflammation

**Target:**
MDM-2/p53;Aryl Hydrocarbon Receptor

**Form:**
White to off-white (Solid)

**Purity / Grade:**
95.42%

**Solubility:**
inVitro : DMSO : ≥ 50 mg/mL (136.13 mM)

**Storage Instruction:**
Powder : -20°C for 3 years 4°C for 2 years In solvent : -80°C for 6 months -20°C for 1 month

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**Alternative Names:**
Pifithrin hydrobromide;PFTα hydrobromide

**Observed Molecular Weight:**
367.3

## 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.

## Product Description

Pifithrin-α hydrobromide is an inhibitor of p53, also acts as an aryl hydrocarbon receptor (AhR) agonist.

IC50 & Target: p53AhR[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 geneCYP1A1.

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
Kinetic 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 [3H]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 [3H]TCDD alone[2]Cell Assay: Pifithrin-α is prepared in DMSO and stored, and then diluted with appropriate media before use[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% CO2. 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] .

Animal Administration: Pifithrin-α is prepared in PBS (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.