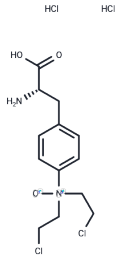
Data Sheet (Cat.No.T6961)

TargetMol

PX-478

Chemical Properties



CAS No. : 685898-44-6

Formula: C13H20Cl4N2O3

Molecular Weight: 394.12

Storage: Store under nitrogen,Keep away from moisture,Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PX-478 is a HIF-1α inhibitor with selectivity, oral activity, and blood-brain barrier permeability. PX-478 has antitumor activity and also protects pancreatic β-cell function in diabetes mellitus and is used in type 2 diabetes mellitus research.
Targets(IC50)	HIF/HIF Prolyl-Hydroxylase,HIF,Autophagy
In vitro	**METHODS**: Tumor cells MCF-7, HT-29 and PC-3 were treated with PX-478 under normoxic or hypoxic conditions for 16 h, and then grown under normoxic conditions for another 56 h. Cell viability was detected by MTT assay. **RESULTS**: PX-478 produced a smaller but significantly greater inhibition of cell growth under hypoxic conditions compared to normoxic conditions. the hypoxic/normoxic IC50 of MCF-7 cells was 25.1/20.0 μM, with a ratio of 1.25. the hypoxic/normoxic IC50 of HT-29 cells was 29.5/23.9 μM, with a ratio of 1.20, and that of PC-3 cells was 16.2/11.9 μM, with a ratio of 16.2/11.0 μM. IC50 for PC-3 cells was 16.2/11.1 μM with a ratio of 1.45. [1] **METHODS**: Human prostate cancer cells PC3 and DU 145 were treated with PX-478 (10-40 μM) under normoxic conditions for 20 h. The expression levels of target proteins were detected by Western Blot. **RESULTS**: Under normoxic conditions, the IC50 of PX-478 for HIF-1α inhibition in PC3 cells was 20-25 μM (ΔHIF:0.56±0.08), while the IC50 of HIF1α inhibition in DU 145 cells was 40-50 μM (ΔHIF:0.47±0.08). [2]
In vivo	**METHODS**: To study the activity on metabolism in vivo, PX-478 (5 mg/kg) was administered by gavage to C57BL/6 mice on a high-fat diet (HFD) every two days for seven weeks. **RESULTS**: PX-478 treatment effectively inhibited HFD-induced HIF1α activation in adipose tissue. Inhibition of HIF1α in adipocytes significantly improved metabolism. [3] **METHODS**: In order to detect the anti-tumor activity in vivo, PX-478 (75-100 mg/kg) was intraperitoneally injected into scid mice carrying tumors OvCar-3, SHP-77, MCF-7, or PC-3 once a day for five days. **RESULTS**: PX-478 showed antitumor activity against established human tumor xenografts. [4]
Cell Research	PX-478 is prepared as a 10 mM stock in distilled water and used immediately[1]. To determine the effect of PX-478 in combination with radiation, cells are treated with PX-478 for 24 hr under normoxic condition, irradiated and plated after 1 hr. Colonies are

Cell Research	stained with crystal violet after 12 days and the colonies of >50 cells are counted. For combination treatments, net survival is calculated by correcting the toxicity of PX-478 alone. Enhancement factor (EF) is calculated by dividing the dose of radiation required to reduce plating efficiency to 10% when cells are treated with radiation alone by the dose of radiation required to reduce plating efficiency to 10% when cells are treated with PX-478 and radiation[1].

Solubility Information

Solubility	DMSO: 50 mg/mL (126.86 mM),Sonication is recommended. H2O: 88.81 mM,Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5 mg/mL (12.69 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5373 mL	12.6865 mL	25.373 mL
5 mM	0.5075 mL	2.5373 mL	5.0746 mL
10 mM	0.2537 mL	1.2686 mL	2.5373 mL
50 mM	0.0507 mL	0.2537 mL	0.5075 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Koh MY, et al. Molecular mechanisms for the activity of PX-478, an antitumor inhibitor of the hypoxia-inducible factor-1alpha. Mol Cancer Ther. 2008 Jan;7(1):90-100.
Chang L L, Lu P H, Yang W, et al. AKR1C1 promotes non-small cell lung cancer proliferation via crosstalk between HIF-1α and metabolic reprogramming. Translational Oncology. 2022, 20: 101421
Liu R, Tian Y, Wang J, et al.Visible light-initiated radical 1,3-difunctionalization of β, γ-unsaturated ketones.Science Advances.2022, 8(49): eabq8596.
Palayoor ST, et al. PX-478, an inhibitor of hypoxia-inducible factor-1alpha, enhances radiosensitivity of prostate carcinoma cells. Int J Cancer. 2008 Nov 15;123(10):2430-7.
Sun K, et al. Selective inhibition of hypoxia-inducible factor 1α ameliorates adipose tissue dysfunction. Mol Cell Biol. 2013 Mar;33(5):904-17.
Welsh S, et al. Antitumor activity and pharmacodynamic properties of PX-478, an inhibitor of hypoxia-inducible factor-1alpha. Mol Cancer Ther. 2004 Mar;3(3):233-44.

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