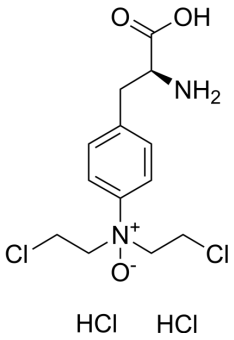
PX-478

Cat. No.:	HY-10231
CAS No.:	685898-44-6
Molecular Formula:	$C_{13}H_{20}Cl_4N_2O_3$
Molecular Weight:	394.12
Target:	HIF/HIF Prolyl-Hydroxylase; Autophagy
Pathway:	Metabolic Enzyme/Protease; Autophagy
Storage:	-20°C, stored under nitrogen, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (253.73 mM; Need ultrasonic)

H_2O : ≥ 35 mg/mL (88.81 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent, Mass	1 mg	5 mg	10 mg
1 mM	2.5373 mL	12.6865 mL	25.3730 mL
5 mM	0.5075 mL	2.5373 mL	5.0746 mL
10 mM	0.2537 mL	1.2686 mL	2.5373 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: Saline
   Solubility: 16.67 mg/mL (42.30 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5 mg/mL (12.69 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (12.69 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (12.69 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (6.34 mM); Clear solution
6. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.34 mM); Clear solution
7. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: ≥ 0.5 mg/mL (1.27 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	PX-478 is an orally active HIF-1α inhibitor with potent antitumor activities. PX-478 can cross the blood-brain barrier[1][2].
IC_{50} & Target	HIF-1α[1]
In Vitro	PC3 and DU 145 cells express HIF-1α protein are treated with PX-478 for 20 hr under normoxia. PC3 cells are more sensitive to PX-478 as compared with DU 145 cells. Densitometric analysis shows that the IC_{50} for HIF-1α inhibition for PC3 cells under normoxic condition is 20-25 μM, whereas the IC_{50} for HIF-1α inhibition for the DU 145 cells is 40-50 μM. PC3 and DU 145 cells are treated with different concentrations of PX-478 (10, 20, 30, 40, 50, and 60 μM) for 18-20 hr under normoxia or hypoxia. Under normoxia, PC3 cells are more sensitive to PX-478 than DU 145 cells. IC_{50} for clonogenic survival (n=3) is 17 μM for PC3 cells and 35 μM for DU 145 cells. When cells are treated with the drug under hypoxic condition for 18 hr, the IC_{50} is 16 μM for PC3 cells and 22 μM for DU 145 cells. Thus DU 145 cells are more sensitive to PX-478 under hypoxic condition[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PX-478 is administered to mice with congenital heart disease (Nfatc1-Cre/caACVR1$^{fl/fl}$) every other day starting from birth for 2 wk. Treated mice have significantly less ectopic bone at the ankle joints compared with mutant mice treated with vehicle (6.8 mm^3 vs. 2.2 mm^3, $P<0.01$)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [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 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Burn/tenotomy or hybrid HO mice are administered PX-478 (100 mg/kg) or Rapamycin (5 mg/kg) in PBS solution via intraperitoneal injection. Mice receive injections every other day for the duration of the study. Nfatc1-Cre/caACVR1$^{fl/wt}$ mice are administered PX-478 (100 mg/kg) every other day for a total of 2 wk. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Circulation. 2020 Jul 28;142(4):384-400.
- Sci Transl Med. 2020 Apr 8;12(538):eaay1620.
- Acta Pharm Sin B. 2023 Oct 28.
- Acta Pharm Sin B. 14 October 2021.
- Proc Natl Acad Sci U S A. 2024 Jan 9;121(2):e2315898120.

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REFERENCES

[1]. 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):2430-2437.

[2]. Agarwal S, et al. Inhibition of Hif1α prevents both trauma-induced and genetic heterotopic ossification. Proc Natl Acad Sci U S A. 2016 Jan 19;113(3):E338-47.

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