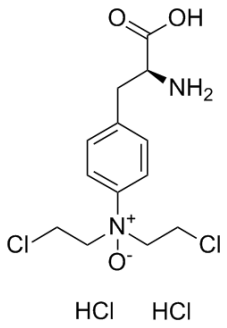
PX-478

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



Solvent & Solubility

In Vitro

H_2O : ≥ 35 mg/mL (88.81 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	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.

BIOLOGICAL ACTIVITY

Description

PX-478 is an inhibitor of hypoxia-inducible factor-1α (**HIF-1α**), and is cytotoxic to a variety of cancer cell lines under normoxia and hypoxia in vitro with **IC_{50}** of 20-30 μM.

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].

In Vivo	PX-478 is administered to mice with congenital HO (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].

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

- **Front Immunol**. 2018 Jul 23;9:1667.
- **Mol Nutr Food Res**. 2018 Jun 23:e1800164.
- **J Biol Chem**. 2017 Jun 30;292(26):11009-11020.

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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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