PDK4-IN-1 hydrochloride

Cat. No.: HY-135954A

CAS No.: 2310262-11-2

Molecular Formula: $C_{22}H_{20}ClN_3O_2$

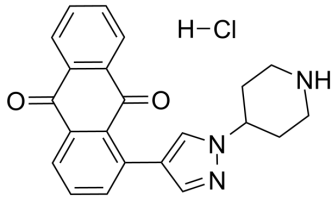
Molecular Weight: 393.87

Target: PDHK; Apoptosis

Pathway: Metabolic Enzyme/Protease; Apoptosis

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 : 100 mg/mL (253.89 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5389 mL	12.6945 mL	25.3891 mL
	5 mM	0.5078 mL	2.5389 mL	5.0778 mL
	10 mM	0.2539 mL	1.2695 mL	2.5389 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: ≥ 2.08 mg/mL (5.28 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PDK4-IN-1 hydrochloride is an anthraquinone derivative and a potent and orally active pyruvate dehydrogenase kinase 4 (PDK4) inhibitor with an IC_{50} value of 84 nM. PDK4-IN-1 hydrochloride potently represses cellular transformation and cellular proliferation and induces apoptosis. PDK4-IN-1 hydrochloride has antidiabetic, anticancer and anti-allergic activity[1].

IC_{50} & Target

IC50: 84 nM (Pyruvate dehydrogenase kinase 4 (PDK4))[1]

In Vitro

PDK4-IN-1 (Compound 8c; 50 μM; 0-72 hours; HCT116 and RKO cells) treatment significantly impedes the proliferation of human colon cancer cell lines, HCT116 and RKO. The colony formation efficiency in HCT116 and RKO cells Is significantly reduced after treatment of PDK4-IN-1[1].

PDK4-IN-1 (Compound 8c; 10-50 μM; 24 hours; HCT116 and RKO cells) treatment dose-dependently increased apoptosis[1].

PDK4-IN-1 (Compound 8c; 10 μM; 24 hours; HEK293T cells) treatment inhibits phosphorylation of Ser^{232}, Ser^{293}, and Ser^{300}

of PDHE1α[1].
10 μM of PDK4-IN-1 (Compound 8c) significantly increases p-Akt in AML12 cells[1].
PDK4-IN-1 (compound 8c)-induced phosphorylation of p53 on serine 15 is a dose-dependent response in both HCT116 and RKO cells. PDK4-IN-1 decreases the expression of BCL-xL and increases the expression of BAX. Cleavage of PARP1 and caspase 3 are increased by PDK4-IN-1[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	HCT116 and RKO cells
Concentration:	50 μM
Incubation Time:	0 hour, 24 hours, 48 hours, 72hours
Result:	Significantly impeded the proliferation of human colon cancer cell lines, HCT116 and RKO.

Apoptosis Analysis[1]

Cell Line:	HCT116 and RKO cells
Concentration:	10 μM, 25 μM, 50 μM
Incubation Time:	24 hours
Result:	Dose-dependently increased apoptosis.

Western Blot Analysis[1]

Cell Line:	HEK293T human embryonic kidney cells
Concentration:	10 μM
Incubation Time:	24 hours
Result:	Inhibited phosphorylation of Ser^{232}, Ser^{293}, and Ser^{300} of PDHE1α.

In Vivo

PDK4-IN-1 (Compound 8c; 100 mg/kg; oral administration; daily; for 1 week; C57BL/6J mice) treatment significantly improves glucose tolerance[1].
Pre-incubation with PDK4-IN-1 (compound 8c) dose-dependently inhibits the release of β-hexosaminidase from IgE/antigen-activated BMMCs, showing that the absorbance values are 0.26, 0.20, and 0.126 in IgE/Ag, 10 μM, and 20 μM PDK4-IN-1-treated BMMCs[1].
The pharmacokinetic (PK) profiles of PDK4-IN-1 (compound 8c) are evaluated in rat. PDK4-IN-1 shows good bioavailability (64%), long half-life (>7 h), and moderate clearance (CL of 0.69) in rats[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6J mice (8-week old) fed with high-fat diet[1]
Dosage:	100 mg/kg
Administration:	Oral administration; daily; for 1 week
Result:	Significantly improved glucose tolerance.

CUSTOMER VALIDATION

- Aging Cell. 2023 Feb 16;e13800.

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REFERENCES

[1]. Lee D, et al. Discovery of Novel Pyruvate Dehydrogenase Kinase 4 Inhibitors for Potential Oral Treatment of Metabolic Diseases. J Med Chem. 2019 Jan 24;62(2):575-588.

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