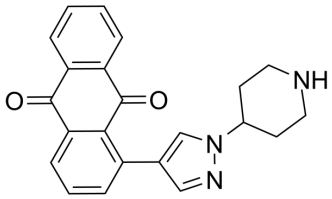
PDK4-IN-1

Cat. No.:	HY-135954
CAS No.:	2310262-10-1
Molecular Formula:	$C_{22}H_{19}N_3O_2$
Molecular Weight:	357.41
Target:	PDHK; Apoptosis
Pathway:	Metabolic Enzyme/Protease; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	PDK4-IN-1 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 potently represses cellular transformation and cellular proliferation and induces apoptosis. PDK4-IN-1 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.

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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