PHD2-IN-1

Cat. No.: HY-155009

CAS No.: 2768219-28-7

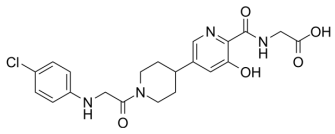
Molecular Formula: $C_{21}H_{23}ClN_4O_5$

Molecular Weight: 446.88

Target: HIF/HIF Prolyl-Hydroxylase

Pathway: Metabolic Enzyme/Protease

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PHD2-IN-1 is a potent and orally active inhibitor of HIF prolyl hydroxylase 2 (PHD2) with an IC_{50} of 22.53 nM. PHD2-IN-1 can be used for anemia research[1].

In Vitro

PHD2-IN-1 (Compound 22) (0-50 μM; 12 hours) stabilizes HIF-α and increases the expression of the erythropoietin (EPO) gene [1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

RT-PCR[1]

Cell Line:	Hep3B cells
Concentration:	0,5,20,50 μM
Incubation Time:	12 hours
Result:	Significantly stabilized HIF-1α and HIF-2α. Upregulated the EPO mRNA level in a dose-dependently manner. Showed no significant effects on the expression of the VEGFA gene.

In Vivo

PHD2-IN-1 (Compound 22) (10,20,50 mg/kg, p.o., once daily for three days) stimulates erythropoiesis and increase reticulocytes in a dose-dependent manner in C57BL/6 mice[1].

PHD2-IN-1 (50,100,200 mg/kg for i.p., once daily for 14 days) has no significant toxic reactions in ICR mice[1].

PHD2-IN-1 (1 mg/kg for i.p., 10 mg/kg for p.o.) shows $T_{1/2}$s of 2.29 h (p.o.) or 3.72 h (i.v.) in rats and 1.17 h (p.o.) or 0.33 h (i.v.) in mice. And oral bioavailability (F%) of 33.9% in rats and 35.3% in mice[1].

Pharmacokinetic parameters for PHD2-IN-1 (Compound 22) in SD rats and C57BL/6 mice [1]

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Species	Route	Dose (mg/kg)	T_{max} (h)	C_{max} (ng/mL)	AUC_{0-t} (h•ng/mL)	$AUC_{0-\infty}$ (h•ng/mL)	$T_{1/2}$ (h)	CL (mL•min^{-1}/kg^{-1})	V_Z (mL/kg)	$MRT_{0-\infty}$ (h)	F (%)
rat	p.o.	10	0.08	26140	7118	7135	2.29	1417	4629	0.56	33.9

rat	i.v.	1	/	/	2069	2106	3.72	483	2644	1.54	/
mice	p.o.	10	0.5	3036	4475	4489	1.17	2246	4532	1.67	35.3
mice	i.v.	1	/	/	1384	1387	0.33	721	345	0.53	/

Animal Model:	C57BL/6 mice[1]
Dosage:	10,20, and 50 mg/kg
Administration:	Oral gavage (p.o.), once daily for three days
Result:	Increased reticulocytes in a dose-dependent manner. The reticulocyte count/red blood cell count (RBC%) increased significantly in a dose-dependent manner.

Animal Model:	SD rats and C57BL/6 mice (Pharmacokinetic assay)[1]
Dosage:	1, 10 mg/kg
Administration:	Intravenous injection (i.v.)、Oral gavage (p.o.)
Result:	Showed $T_{1/2}$s of 2.29 h (p.o.) or 3.72 h (i.v.) in rats and 1.17 h (p.o.) or 0.33 h (i.v.) in mice. And oral bioavailability (F%) of 33.9% in rats and 35.3% in mice.

Animal Model:	Subacute toxicity assessment in ICR mice[1]
Dosage:	50,100,200 mg/kg
Administration:	Intraperitoneal injection (i.p.) once daily for 14 days
Result:	Had no significant hepatotoxicity or nephrotoxicity reactions after administration of a high dose of 200 mg/kg, at 10 imes the efficacious dose (20mg/kg). Observed no death or behavioral abnormalities when the mice were treated in the dose of 800 mg/kg by p.o. administration.

REFERENCES

[1]. Wu Y, et.al. Preferred Conformation-Guided Discovery of Potent and Orally Active HIF Prolyl Hydroxylase 2 Inhibitors for the Treatment of Anemia. J Med Chem. 2023 Jul 13;66(13):8545-8563.

Caution: Product has not been fully validated for medical applications. For research use only.

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