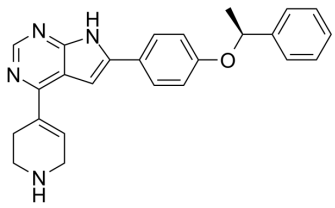
PRMT5-IN-19

Cat. No.:	HY-149005
CAS No.:	2783961-86-2
Molecular Formula:	$C_{25}H_{24}N_4O$
Molecular Weight:	396.48
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description PRMT5-IN-19 (Compound 41) is an selective orally active non-nucleoside PRMT5 inhibitor with IC_{50} values of 23.9 nM (radioactive biochemical assay assay). PRMT5-IN-19 can occupy the SAM-binding pocket in PRMT5 and block methyltransferase activity, which displays good selectivity over other IN-19 inhibits cell proliferation by inducing cell apoptosis, and can be used for cancer-related research[1].

IC_{50} & Target	PRMT5	PRMT1	PRMT4
	23.9 nM (IC_{50})	3.252 μM (IC_{50})	>20 μM (IC_{50})

In Vitro

PRMT5-IN-19 (Compound 41, 5 days) has strong anti-proliferative effects against the A375 cell with an IC_{50} value of 1.36 μM[1].
PRMT5-IN-19 shows higher selectivity for PRMT5 (IC_{50} value of 23.9 nM) than other histone methyltransferases (PRMT1 and PRMT4), and PKMTS (EZ .
PRMT5-IN-19 binds with the SAM-binding pocket in PRMT5[1].
PRMT5-IN-19 (4-5 days) Inhibits proliferation of multiple cancer cell lines (A-375, CHL-1, SNU-423, SNU-449, MDA-MB-231, MDA-MA-453, MV-4-11, MC ranging from 1.08 to 3.45 μM[1].
PRMT5-IN-19 inhibits arginine symmetrical dimethylation in A375 cells [1].
PRMT5-IN-19 (0-4 μM, 48 h) suppresses A375 cell proliferation by inducing apoptosis in a concentration-dependent manner[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	A-375, CHL-1, SNU-423, SNU-449, MDA-MB-231, MDA-MA-453, MV-4-11, MOLM13
Concentration:	0-10 μM
Incubation Time:	5 days
Result:	Inhibited proliferation of multiple cancer cell lines with IC_{50} value ranging from 1.08 to 3.45 μM.

Western Blot Analysis[1]

Cell Line:	A-375 cells
Concentration:	0.5, 1, 2, 4,8 μM
Incubation Time:	48 h.
Result:	Inhibited arginine symmetrical dimethylation in a dose-dependent manner.

In Vivo

PRMT5-IN-19 (Compound 41, A375 xenograft model, 75 mg/kg/d, p.o., 19 days) has good PK properties and significant antitumor efficacy, without t weight and visible toxicity[1].

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

Animal Model:	A375 cell-derived nude mouse xenograft model[1].
Dosage:	75 mg/kg/d
Administration:	P.o., 19 days
Result:	Had no effect on the body weight, displayed antitumor efficacy with a tumor growth inhibition (TGI) rate of 7 methyltransferase activity of PRMT5.

Animal Model:	Rats and mice[1].
Dosage:	10 mg/kg for p.o., 3 mg/kg for i.v
Administration:	P.o., i.v. (Pharmacokinetic Analysis)
Result:	Pharmacokinetic parameters for PRMT5-IN-19 in SD Rats and Mice[a,c] [1].

species	PRMT5-IN-19	$T_{1/2}$ (h)	$C_{max\ (ng/mL)}$	CL (mL/min/kg)	F (%)
rat	iv (3 mg/kg)/td>	2.58		310	
	po (10 mg/kg)/td>	7.51	8.22		7.25
	po (10 mg/kg)/td>	2.95	27.7		23.7
mouse	iv (3 mg/kg)/td>	4.71		153	
	po (10 mg/kg)/td>		128		

REFERENCES

[1]. Deqin Rong, et al. Structure-Aided Design, Synthesis, and Biological Evaluation of Potent and Selective Non-Nucleoside Inhibitors Targetin Methyltransferase 5. J Med Chem. 2022 Jun 9;65(11):7854-7875.

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