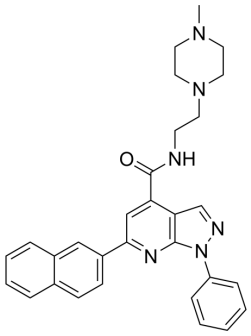
KDM5B-IN-4

Cat. No.:	HY-149091
Molecular Formula:	$C_{30}H_{30}N_6O$
Molecular Weight:	490.6
Target:	Others
Pathway:	Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	KDM5B-IN-4 (compound 11ad) is a lysine demethylase 5B (KDM5B) inhibitor with an IC_{50} of 0.025 μM KDM5B-IN-4 increases substrate H3K4me1/2/3 level by inhibiting KDM5B in PC-3 cells. KDM5B-IN-4 downregulates PI3K/AKT. KDM5B-IN-4 reduces tumor volume in mice and shows less toxic to organs[1].
IC_{50} & Target	IC 50: 0.025 μM (Lysine demethylase 5B, KDM5B)[1].

In Vitro

KDM5B-IN-4 (20 μM, 72 h) has targeted inhibition of KDM5B and induction of H3K4me1/2/3 production in PC-3 cells[1].
KDM5B-IN-4 (0-20 μM; 72 h) not only targets KDM5B in cells, but also induces H3K4me1/2/3 accumulation in PC-3 cells[1].
KDM5B-IN-4 (0-10 μM, 0-24 h) inhibited the proliferation and migration of prostate cancer cells, blocked the PC-3 cycle in the G2/M phase, and induced apoptosis of PC-3 cells to a certain extent[1].

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

Western Blot Analysis[1]

Cell Line:	PC-3
Concentration:	0, 2.5, 5, 10, 20 μM
Incubation Time:	72 h
Result:	Induced the concentrations of H3K4me1/2/3 significantly different from those of the control, and the results obtained were similar to those obtained using the CPI-455 positive control. Had no significant effect on P110α, P85, and pAKT at low concentration levels (0-10μM), and P110α, P85, and pAKT were significantly decreased when 11ad was at high concentration (20 μM).

Cell Migration Assay [1]

Cell Line:	PC-3
Concentration:	0, 5, 10 μM
Incubation Time:	0, 6, 12, 24 h
Result:	Inhibited colony formation in a dosedependent manner, especially at high doses (10 μM).

Cell Cycle Analysis[1]

Cell Line:	PC-3
Concentration:	0, 2.5, 5, 10 μM
Incubation Time:	24 h
Result:	Blocked the cell cycle at G2/M phase in 10 μM.

Apoptosis Analysis[1]

Cell Line:	PC-3
Concentration:	0, 2.5, 5, 10 μM
Incubation Time:	24 h
Result:	Induced PC-3 cell apoptosis in a dose-dependent manner (7.58%, 26.14%, 28.20%, 45.66%).

In Vivo

KDM5B-IN-4 (50 mg/kg, i.g., 50 mg/kg/d, 13 days) treatment at 50 mg/kg was slightly better than the efficacy of DOX[1].
KDM5B-IN-4 (50 mg/kg, i.g., 50 mg/kg/d, 25 days) did not cause noticeable damage to the mice, confirming that 11ad had no significant toxicity or side effects in vivo[1].
Pharmacokinetic Analysis in KDM5B-IN-4 (compound 11ad) Xenograft Model[1]

KDM5B-IN-4 (compound 11ad) [redacted][1]

Parameter	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	AUC_{0-t} (h*ng/mL)	MRT_{0-t} (h)	V_z (L/kg)	Cl (L•h/kg)	F
p.o. (25mg/kg)	5.30	6.0	411.67	3024.33	6.90	/	/	20.28%
i.v. (5mg/kg)	2.95	0.083	551.67	44437.67	10.29	19.51	0.49	/

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Animal Model:	PC-3 xenograft model in male Spraguee-Dawley rats[1].
Dosage:	25, 50 mg/kg
Administration:	Intragastric administration to mice (i.g.) for 25 days, administered once daily.
Result:	Compared with NaCl treatment, treatment with 25 mg/kg and 50 mg/kg significantly decreased tumor volume.

Animal Model:	PC-3 xenograft model in male Spraguee-Dawley rats[1].
Dosage:	2 g/kg
Administration:	Intragastric administration to mice (i.g.) for 14 days, administered once daily.
Result:	No significant loss of major organs in the high-dose and low-dose groups.

REFERENCES

[1]. Cao Y, et al. Discovery of a novel 1H-pyrazole- [3,4-b] pyridine-based lysine demethylase 5B inhibitor with potential anti-prostate cancer activity that perturbs the phosphoinositide 3-kinase/AKT pathway. Eur J Med Chem. 2023 May 5;251:115250.

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