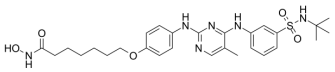
JAK/HDAC-IN-2

Cat. No.:	HY-149283
CAS No.:	3029138-43-7
Molecular Formula:	$C_{28}H_{38}N_6O_5S$
Molecular Weight:	570.7
Target:	JAK; HDAC; Apoptosis
Pathway:	Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt; Cell Cycle/DNA Damage; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

JAK/HDAC-IN-2 is a potent 2-amino-4-phenylaminopyrimidine JAK/HDAC dual-target inhibitor. JAK/HDAC-IN-2 potently inhibits HDAC3/6 and JAK1/2 at nanomolar levels. JAK/HDAC-IN-2 has proapoptotic activity and inhibits histone deacetylation and STAT3 phosphorylation. JAK/HDAC-IN-2 presents remarkable antiproliferative activity in both hematological malignancies and solid cancers[1].

IC_{50} & Target

JAK2 5.32 nM (IC_{50})	JAK1 27.15 nM (IC_{50})	JAK3 594.8 nM (IC_{50})	Tyk2 414.4 nM (IC_{50})
HDAC 170 nM (IC_{50})	HDAC1 340 nM (IC_{50})	HDAC2 303 nM (IC_{50})	HDAC3 58.7 nM (IC_{50})
HDAC6 4.44 nM (IC_{50})	HDAC10 116.1 nM (IC_{50})	HDAC11 724.4 nM (IC_{50})	HDAC4 >10000 nM (IC_{50})
HDAC5 >10000 nM (IC_{50})	HDAC7 >10000 nM (IC_{50})	HDAC8 >10000 nM (IC_{50})	HDAC9 >10000 nM (IC_{50})

In Vitro

JAK/HDAC-IN-2 (compound 21) exhibits great antiproliferative activities against K562, HL-60, and HEL cells (IC_{50}=1.87, 2.26, and 0.33 μM, respectively). JAK/HDAC-IN-2 inhibits the proliferation of four solid tumor cells, MCF-7, HeLa, A549, and PC-3 (IC_{50}=1.83, 2.88, 0.73, and 2.52 μM, respectively)[1].

JAK/HDAC-IN-2 (1, 5 μM; 24 h) possesses excellent proapoptotic activity in HEL cells and moderate proapoptotic activity in A549 cells[1].

JAK/HDAC-IN-2 (1, 5 μM; 24 h) significantly induces the inhibition of histone deacetylation and STAT3 phosphorylation in hematological malignancy HEL cells as well as solid tumor A549 cells by inhibiting both HDAC and JAK[1].

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

Apoptosis Analysis[1]

Cell Line:	HEL cells
Concentration:	1, 5 μM
Incubation Time:	24 h

Result:	The apoptotic rates were 37.6% at 1 μM and 81.5% at 5 μM on HEL cells.

Western Blot Analysis[1]

Cell Line:	A549 and HEL cells
Concentration:	1, 5 μM
Incubation Time:	24 h
Result:	Bviously upgraded the expression level of acetyl-H3 and acetyl-tubulin in A549 cells in a dose-dependent manner. Reduced the expression level of p-STAT3-Tyr705.

In Vivo

JAK/HDAC-IN-2 (compound 21; 50 mg/kg; Intraperitoneally; once a day for 18 consecutive days) exhibits effective antitumor activity in vivo against hematological malignancy HEL and solid tumors A549[1].

Pharmacokinetic Parameters of LSD1-IN-14 in male Sprague-Dawley rats[1].

	IV (3 mg/kg)	PO (15 mg/kg)
T_{max} (h)		2.912
C_{max} (ng/mL)		93.328
AUC_{0-t} (ng/mL*h)	656.241	745.249
$t_{1/2}$ (h)	0.128	2.084
CL (L/ kg*h)	4.571	4.56
V_{ss} (L/kg)	0.845	
F (%)		22.71%

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Animal Model:	C57BL/6 nude mice[1]
Dosage:	50 mg/kg
Administration:	Intraperitoneally; once a day for 18 consecutive days
Result:	Prominently reduced the weight and volume of HEL and A549 xenografts. Upgraded the expression level of acetyl-H3 as well as acetyl-tubulin and reduced the expression level of p-STAT3-Tyr705 in HEL as well as A549 xenograft tumor tissues.

REFERENCES

[1]. Qianqian Qiu, et al. Exploration of Janus Kinase (JAK) and Histone Deacetylase (HDAC) Bispecific Inhibitors Based on the Moiety of Fedratinib for Treatment of Both Hematologic Malignancies and Solid Cancers. J Med Chem. 2023 Apr 27;66(8):5753-5773.

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

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