Tubulin/HDAC-IN-1

Cat. No.: HY-150772

CAS No.: 2413587-26-3

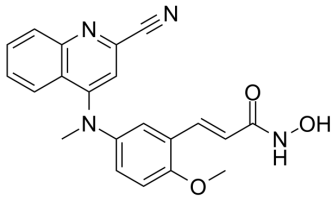
Molecular Formula: $C_{21}H_{18}N_4O_3$

Molecular Weight: 374.39

Target: Microtubule/Tubulin; HDAC; Apoptosis; Mitochondrial Metabolism

Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Epigenetics; Apoptosis; Metabolic Enzyme/Protease

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



BIOLOGICAL ACTIVITY

Description

Tubulin/HDAC-IN-1 is a dual tubulin and HDAC-IN-1 inhibitor through CH/π interaction with tubulin and hydrogen bond interaction with HDAC8. Tubulin/HDAC-IN-1 inhibits tubulin polymerization and selectively inhibits HDAC8 (IC_{50}: 150 nM). Tubulin/HDAC-IN-1 has cytotoxicity against various human cancer cells, also arrests cell cycle in the G2/M phase and induces cell apoptosis. Tubulin/HDAC-IN-1 can be used in the research of hematologic and solid tumors such as neuroblastoma, leukemia[1].

IC_{50} & Target	HDAC8	HDAC6	HDAC11
	150 nM (IC_{50})	1 μM (IC_{50})	1.9 μM (IC_{50})

In Vitro

Tubulin/HDAC-IN-1 (Compound 12a, 72 h) shows cytotoxicity against various human cancer cell lines with an averaged IC_{50} value of 0.6 nM[1].

Tubulin/HDAC-IN-1 (2 nM, 24 h) induces HT29 cell cycle arrest in the G2/M phase and produces caspase-induced apoptosis of HT29 cells through mitochondrial dysfunction[1].

Tubulin/HDAC-IN-1 selectively inhibits HDAC8 (IC_{50}: 150 nM), inhibits HDAC6 and HDAC11 with IC $_{50}$ values of 1 μM and 1.9 μM respectively[1].

Tubulin/HDAC-IN-1 (0.5-100 nM, 24 h/30 min) dose-dependently increases γH2AX level and acetylated SMC3 in HT-29 cells[1].

Tubulin/HDAC-IN-1 (5-15 μM, 0-40 min) inhibits tubulin polymerization in a dose-dependent manner, with a maximal effect achieved at 10 μM[1].

Tubulin/HDAC-IN-1 (250 nM, 30 min) depolymerizes the cell microtubule network, and the effect is not specific[1].

Tubulin/HDAC-IN-1 shows good in vitro metabolic stability expressed by the intrinsic clearance CLint (given in μL/min/mg protein) using rat liver microsomes (RLM) and human liver microsomes (HLM)[1].

Compound	RLM	RLM	HLM	HLM
	$t_{1/2}$ (h)	CL_{int}	$t_{1/2}$	CL_{int}
Tubulin/HDAC-IN-1	6.6	1.75	32	0.36

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

Cell Proliferation Assay[1]

Cell Line:	Various tumor cell lines as below
Concentration:	
Incubation Time:	72 h
Result:	Activities of Tubulin/HDAC-IN-1 (Compound 12a) against various tumor cell lines (IC_{50} nM):

	NCIN87	K562	K562R	MiaPaca2	SKOV3	A549	MCF-7	MDA-MB-231	HCT116	HT-29
Tubulin/HDAC-IN-1	0.1	0.35	0.56	0.94	0.6	0.84	0.78	0.7	0.6	0.62

Western Blot Analysis[1]

Cell Line:	HT-29 cells
Concentration:	0.5, 1, 5, 10 nM for γH2AX; 0.5, 1, 100 nM for acetylated SMC3
Incubation Time:	24 h for γH2AX, 30 min for acetylated SMC3
Result:	Dose-dependently increased γH2AX level and acetylated SMC3.

In Vivo

Tubulin/HDAC-IN-1 (Compound 12a, intratumoral injection, 0.25 mg/kg, three times a week for two weeks) decreases MCA205 tumor growth and extends the overall survival of treated mice in allogeneic sarcoma mice model[1].

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

Animal Model:	Allogeneic sarcoma model in C57BL/6 mice[1]
Dosage:	0.1, 0.25, 0.50 mg/kg, three times a week for two weeks.
Administration:	Intratumoral injection
Result:	Decreased tumor growth and extended the overall survival of treated mice with no obvious side effects.

REFERENCES

[1]. Camille Hauguel, et al. Design, synthesis and biological evaluation of quinoline-2-carbonitrile-based hydroxamic acids as dual tubulin polymerization and histone deacetylases inhibitors. Eur J Med Chem. 2022 Jul 1;240:114573.

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