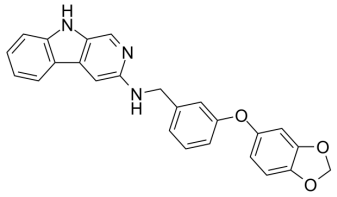
αβ-Tubulin-IN-1

Cat. No.:	HY-144132
CAS No.:	2478584-74-4
Molecular Formula:	$C_{25}H_{19}N_3O_3$
Molecular Weight:	409.44
Target:	Apoptosis; Microtubule/Tubulin
Pathway:	Apoptosis; Cell Cycle/DNA Damage; Cytoskeleton
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	αβ-Tubulin-IN-1 is a potent and orally active αβ-Tubulin inhibitor. αβ-Tubulin-IN-1 induces cell cycle arrest at G2/M and efficient apoptosis. αβ-Tubulin-IN-1 inhibits tumor cell migration and Metastasis. αβ-Tubulin-IN-1 shows significant antitumor efficacy in a dose dependent manner[1].
IC_{50} & Target	αβ-Tubulin[1]

In Vitro

αβ-Tubulin-IN-1 (compound 12 b) (0, 0.5, 1, 5, 10, 50 μM; 16 h) promotes αβ-tubulin degradation in a concentration-dependent manner in Hela and K562 (0-10 μM) cells[1].
αβ-Tubulin-IN-1 exhibits potent cytotoxic activity toward sensitive cells and resistant cells[1].
αβ-Tubulin-IN-1 (0-300 nM; 48 h) induces cell cycle arrest at G2/M and efficient apoptosis in A2780S and A2780T cells[1].
αβ-Tubulin-IN-1 (0, 1.25, 2.5, 5, 10 nM; 24, 48 h) inhibits tumor cell migration and Metastasis with the inhibition rate of 76.21% and 85.07% for 24 , 48 h in human umbilical vein endothelial cells (HUVEC)[1].

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

Cell Proliferation Assay[1]

Cell Line:	Hela, A2780S, MCF-7, Raji, H460 cells
Concentration:	0-500 nM
Incubation Time:	24 h
Result:	Showed anti-proliferative activity with IC_{50}s of 5, 8, 9,13, 14 nM for Hela, A2780S, MCF-7, Raji, H460 cells, respectively.

Western Blot Analysis[1]

Cell Line:	HeLa cells
Concentration:	10 μM
Incubation Time:	16 h
Result:	Remarkably promoted tubulin degradation by binding to the colchicine site, and the degradation process relied on the ubiquitin−proteasome pathway.

Cell Viability Assay[1]

Cell Line:	A2780S, A2780T, A549, A549T, MCF7, MCF7/ADR cells
Concentration:	
Incubation Time:	24 h
Result:	Exhibited potent cytotoxic activity with IC_{50}s of 16.4, 13.1, 60.1, 63.8, 11.3, 13.5 nM for A2780S, A2780T, A549, A549T, MCF7, MCF7/ADR cells, respectively.

Cell Cycle Analysis[1]

Cell Line:	A2780S (PTX-sensitive), A2780T (PTX-resistant) cells
Concentration:	0, 3, 10, 30, 100, 300 nM
Incubation Time:	48 h
Result:	Induced cell cycle arrest at G2/M phase with the the percentages of A2780S and A2780T cells were 55.10%, 72.18% at 100 nM, and 79.54%, 72.89% at 300 nM.

Apoptosis Analysis[1]

Cell Line:	A2780S, A2780T cells
Concentration:	0, 3, 10, 30, 100, 300 nM
Incubation Time:	48 h
Result:	Induced cell apoptosis with the total numbers of late apoptotic cells were 3.7%, 25.2%, 30.6% at 30,100, and 300 nM, and 5.2% % late apoptotic cells in control.

In Vivo

αβ-Tubulin-IN-1 (5 mg/kg; i.v., p.o.) shows intravenous and oral administration approaches are available in vivo[1].
αβ-Tubulin-IN-1 (10, 20, 40 mg/kg; i.v.; 3 times a week for 2-4 weeks) shows significant antitumor efficacy in a dose dependent manner[1].
Pharmacokinetic Parameters of αβ-Tubulin-IN-1 in rats[1].

route	i.v.	p.o.
dose (mg/kg)	5	5
$T_{1/2}$ (h)	3.57±1.10	4.42±1.90
CL (L/h/kg)	1.52±0.39	5.06±1.70
V_{ss} (L/kg)	8.08±4.19	35.26±25.76
$AUC_{0-\infty}$ (μg/mL·h)	3448.81±782.66	1058.74±285.62
C_{max} (μg/L)	2601.47±444.20	189.29±119.02
F (%)		30.70

Rats, 5 mg/kg for i.v., 5 mg/kg for p.o.[1].

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Animal Model:	Rats[1]
Dosage:	5 mg/kg
Administration:	I.v. or p.o.
Result:	Showed oral bioavailability (F=30.70%) with the T1/2 values for intravenous and oral administration approaches are 3.57 h and 4.42 h, respectively.

Animal Model:	5-6weeks female Balb/C and athymic nude mice (A2780S and A2780T Xenograft) Models[1]
Dosage:	10, 20, 40 mg/kg for i.v., 40 mg/kg for p.o.
Administration:	I.v.; 3 times a week for 2-4 weeks
Result:	Showed significant antitumor efficacy with tumor growth inhibition (TGI) of 66.06%, 71.47% and 92.41% at 10, 20 and 40 mg/kg in A2780S xenograft nude mice model, and 26.94%, 37.2%, 75.73% at 10, 20 and 40 mg/kg in PTX-resistant A2780T xenograft model for i.v. injection, did not show an acceptable antitumor efficacy with 34.93% of TGI at the 40 mg/kg for p.o..

REFERENCES

[1]. Li Y, et al. Structure-Based Design and Synthesis of N-Substituted 3-Amino-β-Carboline Derivatives as Potent αβ-Tubulin Degradation Agents. J Med Chem. 2022 Feb 10;65(3):2675-2693.

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