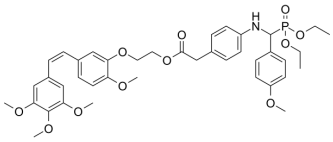
Tubulin/MMP-IN-2

Cat. No.:	HY-152030
CAS No.:	2734877-51-9
Molecular Formula:	$C_{40}H_{48}NO_{11}P$
Molecular Weight:	749.78
Target:	Microtubule/Tubulin; MMP; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton; Metabolic Enzyme/Protease; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Tubulin/MMP-IN-2 is dual inhibitor of tubulin and matrix metalloproteinases. Tubulin/MMP-IN-2 can strongly inhibit tubulin polymerization and induces cell apoptosis. Tubulin/MMP-IN-2 has inhibitory activities against MMP-2, MMP-3 and MMP-9 with IC_{50} values of 24.95 μM, 31.60 μM and 22.37 μM, respectively. Tubulin/MMP-IN-2 can be used for the research of cancer [1].
IC_{50} & Target	IC50: 0.36 μM (HepG-2), 0.31 μM (HT29), 0.19 μM (A549), 0.42 μM (MGC-803), 10.45 μM (LO2 cells); 0.32 μM (SK-OV-3), 0.39 μM (SK-OV-3/CDDP), 0.27 μM (MCF-7), 0.25 μM (MCF-7/DOX); 24.95 μM (MMP-2), 31.60 μM (MMP-3), 22.37 μM (MMP-9)[1].

In Vitro

Tubulin/MMP-IN-2 (Compound 9e) (0.01-20 μM; 24 h) has activity for HepG-2, HT29, A549, MGC-803 and LO2 cells with IC_{50} values of 0.36 μM, 0.31 μM, 0.19 μM, 0.42 μM and 10.45 μM, respectively[1].

Tubulin/MMP-IN-2 has anti-proliferative activities for SK-OV-3, SK-OV-3/CDDP, MCF-7 and MCF-7/DOX cells with IC_{50} values of 0.32 μM, 0.39 μM, 0.27 μM and 0.25 μM, respectively[1].

Tubulin/MMP-IN-2 has inhibitory activities against MMP-2, MMP-3 and MMP-9 with IC_{50} values of 24.95 μM, 31.60 μM and 22.37 μM, respectively[1].

Tubulin/MMP-IN-2 (2.5, 5 Mm; 24 h) strongly inhibits tubulin polymerization, and induced cell apoptosis and cell cycle arrest in G2/M stage, remarkably displayed inhibition of cell migration against A549 cells in vitro[1].

Tubulin/MMP-IN-2 (2.5, 5 Mm; 24 h) can induce apoptosis via mitochondria-dependent apoptosis pathway[1].

Tubulin/MMP-IN-2 (2.5, 5 Mm; 24 h) can also cause ER stress demonstrating as up-regulation express of proteins (CHOP, p-elF2a, and p-PERK)[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	HepG-2, HT-29, A549, MGC-803, SK-OV-3, MCF-7, SK-OV-3/CDDP, MCF-7/DOX and normal liver cells LO2
Concentration:	0.01-20 μM
Incubation Time:	72 h
Result:	Exhibited the most potent activity against various human cancer cells as well as multidrug-resistant tumor cells (A549/CDDP and MCF-7/DOX) and also showed significantly lower cytotoxic activity toward human normal liver cells LO2.

Apoptosis Analysis[1]

Cell Line:	A549 cells
Concentration:	2.5, 5 μM
Incubation Time:	24 h
Result:	Significantly induced apoptosis after 24 h.

Cell Cycle Analysis[1]

Cell Line:	A549 cells
Concentration:	2.5, 5 μM
Incubation Time:	24 h
Result:	Induced a concentration-dependent G2/M stage arrest of A549 cells.

Immunofluorescence[1]

Cell Line:	A549 cells
Concentration:	2.5, 5 μM
Incubation Time:	24 h
Result:	Remarkably induced changes in cell morphology, such as loss of membrane protrusions, disrupted microtubule organization and microtubule depolymerization, respectively.

Western Blot Analysis[1]

Cell Line:	A549 cells
Concentration:	2.5, 5 μM
Incubation Time:	24 h
Result:	Increased the accumulation of CHOP, p-eIF2a and p-PERK. Promoted the expression of pro-apoptotic protein (Bax), and regulated down the level of anti-apoptotic protein (Bcl-2). Increased the levels of caspase-3. Lead p53 obviously up-regulated in a concentration-dependent manner.

Cell Migration Assay [1]

Cell Line:	A549 cells
Concentration:	2.5, 5 μM
Incubation Time:	24 h
Result:	Significantly reduced cell migration in a dose-dependent manner.

In Vivo

Tubulin/MMP-IN-2 (15, 30 mg/kg; every two days for three weeks) displays significant in vivo antitumor efficacy in A549 xenograft models without inducing apparent systemic toxicity[1].

Animal Model:	BALB/c nude mice[1]
Dosage:	15, 30 mg/kg
Administration:	Every two days for three weeks
Result:	Exhibited a dose-dependent inhibitory effect on tumor growth. Exhibited no obvious histopathological changes for the main organ tissues (e.g. heart, liver, spleen, lung and kidney).

REFERENCES

[1]. Xiaochao Huang, et al. Novel combretastatin A-4 derivative containing aminophosphonates as dual inhibitors of tubulin and matrix metalloproteinases for lung cancer treatment. Eur J Med Chem. 2022 Dec 15;244:114817.

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