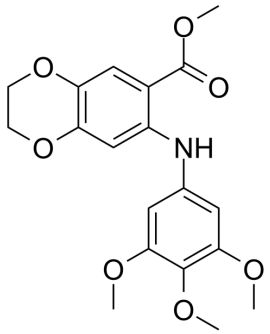
Tubulin polymerization-IN-6

Cat. No.:	HY-146505
CAS No.:	2768613-52-9
Molecular Formula:	$C_{19}H_{21}NO_7$
Molecular Weight:	375.37
Target:	Microtubule/Tubulin; Apoptosis; Reactive Oxygen Species
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton; Apoptosis; Immunology/Inflammation; Metabolic Enzyme/Protease; NF-κB
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Tubulin polymerization-IN-6 (compound 5f) is a potent tubulin polymerization inhibitor, with an IC_{50} of 1.09 μM. Tubulin polymerization-IN-6 inhibits cell migration and tube formation and contributes to the anti-angiogenesis. Tubulin polymerization-IN-6 can greatly inhibit tumor growth on HT29 xenograft Balb/c nude mice[1].
IC_{50} & Target	IC_{50}: 1.09 μM (Tubulin polymerization)[1]

In Vitro

Tubulin polymerization-IN-6 (compound 5f) (0-20 μM, 24 h) shows a broad spectrum of anti-proliferation activity against cancer cell lines[1].

Tubulin polymerization-IN-6 (0-100 nM, 24 h) inhibits tumor cells colony formation, up-regulates the expression of Ac-α-tubulin and DeY-α-tubulin [1].

Tubulin polymerization-IN-6 (0-5 μM, 1 h) competes with colchicine and directly binds to the colchicine binding site, thus inhibit tubulin polymerization[1].

Tubulin polymerization-IN-6 (0-250 nM, 24 h) possesses a favorable anti-migration activity against cancer cells[1].

Tubulin polymerization-IN-6 (0-50 nM, 24 h) has the ability to inhibit the angiogenesis of HUVEC cells[1].

Tubulin polymerization-IN-6 (0-100 nM, 24 h) induces cell cycle arrest by regulating associated proteins, induces apoptosis by regulating associated proteins and down-regulating mitochondrial membrane potential, and dose-dependently promotes the production of ROS in HT29 cells[1].

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

Cell Proliferation Assay

Cell Line:	HT29, MCF-7, HeLa, MDA-MB-231, A549[1]
Concentration:	0-20 μM
Incubation Time:	24 h
Result:	Had a broad spectrum of anti-proliferation activity against cancer cell lines (MCF-7, MDA-MB-231, A549, Hela, and HT29), with IC_{50} values of 0.14 ± 0.03, 0.10 ± 0.00, 0.24 ± 0.03, 0.035 ± 0.002, and 0.023 ± 0.001 μM, respectively; and showed moderate anti-proliferative activity against drug resistant cancer cells (MCF-7/TxR and A549/TxR), with IC_{50} values of 0.18 ± 0.02 and 0.31 ± 0.08 μM, and DRI (drug-resistant index) of 1.3 and 1.2, respectively.

Western Blot Analysis

Cell Line:	HT29 cells[1]
Concentration:	0, 25, 50, and 100 nM
Incubation Time:	24 h
Result:	Up-regulated the expression of Ac-α-tubulin (acetyl-α-tubulin) and DeY-α-tubulin (detyrosinated-α-tubulin); regulated the expressions of the proteins involved in cell cycle such as cdc25c, cdk7, cyclin B1, and cdc2; down-regulated the level of Bim and up-regulated the levels of Bcl-2, p-Bcl-2, and Bax, decreased the expression of p-Histone H3(Ser10) and increased the expression of cleaved-Caspase-9, cleaved-Caspase-3, PARP, and cleaved-PARP.

Immunofluorescence

Cell Line:	HT29 cells[1]
Concentration:	0, 25, 50, and 100 nM
Incubation Time:	6 h
Result:	Dose-dependently depolymerized the tubulin polymers into oligomers, and caused the microtubule network to collapse in HT29 cells.

Cell Cycle Analysis

Cell Line:	HT29 cells[1]
Concentration:	0, 12.5, 25, 50, and 100 nM
Incubation Time:	24 h
Result:	Induced a dose dependent G2/M phase arrest, increased the proportion of G2/M phase cells from 20.9% to 87.5% at 100 nM.

Apoptosis Analysis

Cell Line:	HT29 cells[1]
Concentration:	0, 25, 50, and 100 nM
Incubation Time:	24 h
Result:	Induced apoptosis, increased the percentages of total apoptosis cells, down-regulated mitochondrial membrane potential.

In Vivo

Tubulin polymerization-IN-6 (compound 5f) (HT29 xenograft Balb/c nude mice, 0-10 mg/kg, IP, once every two days, for three weeks) dose-dependently inhibits the tumor growth[1].

Tubulin polymerization-IN-6 (SD rats, 10 mg/kg, IV, once) shows the better pharmacokinetic properties[1].Pharmacokinetic Parameters of Tubulin polymerization-IN-6 in SD rats[1].

Parameters	5f
$t_{1/2}$ (h)	1.73

AUC (μg/L·h)	5.67
MRT (h)	1.92
CL (L/h/kg)	1.76
T_{max} (h)	0.14
C_{max} (ng/mL)	6.88

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

Animal Model:	Immunodeficient Balb/c nude mice (HT29 xenograft, 5-week-old, 36 mice, six groups)[1]
Dosage:	0, 5, 7.5, 10 mg/kg
Administration:	IP, once every two days, for three weeks
Result:	Dose-dependently inhibited the tumor growth, inhibits the tumor weight growth by 75.5% at 10 mg/kg.

Animal Model:	SD rats (5-week-old)[1]
Dosage:	10 mg/kg
Administration:	IV, once (Pharmacokinetic Analysis)
Result:	Showed the better pharmacokinetic properties, exhibited an eight-fold half-life and a two-fold AUC improvement.

REFERENCES

[1]. Yan XY, Leng JF, Chen TT, Zhao YJ, Kong LY, Yin Y. Design, synthesis, and biological evaluation of novel diphenylamine derivatives as tubulin polymerization inhibitors targeting the colchicine binding site. Eur J Med Chem. 2022;237:114372.

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