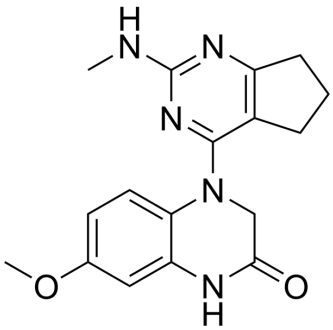
Anticancer agent 98

Cat. No.:	HY-149920
CAS No.:	2857070-72-3
Molecular Formula:	$C_{17}H_{19}N_5O_2$
Molecular Weight:	325.37
Target:	Microtubule/Tubulin
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Anticancer agent 98 (compound 12k) is a microtubule/tubulin-polymerization inhibitor (K_d=16.9 μM). Anticancer agent 98 exerts antiproliferative potency against tumor cells, exhibits anti-angiogenesis effect in vitro. Anticancer agent 98 exhibits good human and mouse liver microsomes stability with both $t_{1/2}$>300 min[1].

In Vitro

Anticancer agent 98 inhibits cancer proliferation among melanoma, breast cancer, and pancreatic cancer with IC50s ranging from 0.6-3 nM[1].
Anticancer agent 98 (300 nM, 1 μM, or 3 μM; 2 h) increases β-tubulin adduct in PC-3 cells dose-dependently[1].
Anticancer agent 98 (3.125, 6.25, 12.5, 25, and 50 μM) has high-binding affinity to tubulin proteins with Kd value of 16.9 μM by SPR spectroscopy assay[1].
Anticancer agent 98 (10 μM, 50 μM; 0-60 min) strongly inhibits tubulin polymerization during 60 min[1].
Anticancer agent 98 (100 nM; 4 h) has antiproliferative and anti-angiogenesis effect on COS-7 cells in vitro[1].

In Vitro Metabolic Stability[1]

human microsomes		mouse microsomes	
$t_{1/2}$ (min)	CL_{int} (μL/min/mg)	$t_{1/2}$ (min)	CL_{int} (μL/min/mg)
>300	<2.31	>300	<2.31

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

In Vivo

Anticancer agent 98 (2.5 mg/kg; i.v.; twice per week for 2 weeks) is well tolerated with no significant weight loss in PC3/TxR xenograft tumors in male NSG mice. Anticancer agent 98 also significantly attenuates the progression of prostate cancer tumors, relative to the Paclitaxel (HY-B0015; 10 mg/kg, once weekly) and control groups[1].

Pharmacokinetic Analysis in NSG Mice[1]

Route	Dose (mg/kg)	C_{max} (ng/mL)	t_{max} (min)	AUC (ng·min/mL)	$t_{1/2}$ (min)	F (%)

i.v.	4	1247	5.0	173,476	238	/
p.o.	10	78.3	10.0	8161	358	2.02

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Animal Model:	PC3/TxR xenograft model in NSG mouse[1]
Dosage:	2.5 mg/kg
Administration:	IV; twice weekly for 2 weeks
Result:	Inhibited the tumor growth in volume by approximately 85.6%. And inhibited angiogenesis by 44% related to control group. Overcame taxane resistance at a low, safe, but potent dose in vivo.

REFERENCES

[1]. Pochampally S, et al. Design, Synthesis, and Biological Evaluation of Pyrimidine Dihydroquinoxalinone Derivatives as Tubulin Colchicine Site-Binding Agents That Displayed Potent Anticancer Activity Both In Vitro and In Vivo[J]. ACS Pharmacology & Translational Science, 2023.

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