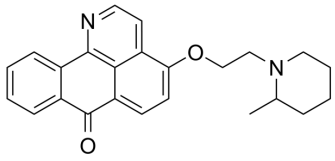
Topoisomerase I inhibitor 5

Cat. No.:	HY-144774
CAS No.:	2513461-95-3
Molecular Formula:	$C_{24}H_{24}N_2O_2$
Molecular Weight:	372.46
Target:	Topoisomerase; DNA/RNA Synthesis; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Topoisomerase I inhibitor 5 is an effective topoisomerase inhibitor with IC_{50} value of. Topoisomerase I inhibitor 5 can interfere with DNA and significantly inhibit the activity of Topoisomerase I. Topoisomerase I inhibitor 5 can arrest cell cycle at the G1 phase and induce MCF-7 cells apoptosis. Topoisomerase I inhibitor 5 has potency in reversing P-gp-mediated resistance to Adriamycin[1].
IC_{50} & Target	Topoisomerase I[1]
In Vitro	Topoisomerase I inhibitor 5 (compound 14) (0-50 μM; 48 hours) exhibits antiproliferation activity against cancer cell lines and lower cytotoxicity in normal cells[1]. Topoisomerase I inhibitor 5 (2-8 μM; 24 hours) induces MCF-7 cell cycle arrest at the G1 phase[1]. Topoisomerase I inhibitor 5 (2-8 μM; 48 hours) increases the apoptotic rate of MCF-7/ADR and MCF-7 cells[1]. Topoisomerase I inhibitor 5 (1.5-6 μM; 24 hours) increases the expression degree of cleaved-caspase-3 and cleaved-PARP in MCF-7; down-regulates the level of anti-apoptotic protein, up-regulates the levels of pro-apoptotic proteins in MCF-7/ADR[1]. Topoisomerase I inhibitor 5 (0.1 μM; 24 hours) induces cell apoptosis by promoting the accumulation of ROS in MCF-7/ADR cell[1]. Topoisomerase I inhibitor 5 (10 μg/ml; 24 hours) increases the accumulation of the ADR and Rh123 in MCF-7/ADR cells[1]. Topoisomerase I inhibitor 5 (5, 10 and 20 μM; 24 hours) reduces the expression degree of P-gp by 14.95% and 18.10% in MCF-7/ADR cells at 10 and 20 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay

Cell Line:	A549, HepG-2, MCF-7, MDA-MB-231, MCF-7/ADR and LO2 cells[1]
Concentration:	0-50 μM
Incubation Time:	48 hours
Result:	Exhibited antiproliferation activity against cancer cell lines, with IC_{50}s of 2.39 ± 0.23 μM, 4.88 ± 0.29 μM, 1.32 ± 0.14 μM, 7.64 ± 0.35 μM and 2.42 ± 0.14 μM in A549, HepG-2, MCF-7, MDA-MB-231, MCF-7/ADR, respectively; and has lower cytotoxicity in LO2 cells with IC_{50} of 36.52 ± 2.36 μM.

Cell Cycle Analysis

Cell Line:	MCF-7[1]
Concentration:	2, 4 and 8 μM
Incubation Time:	24 hours
Result:	Induced MCF-7 cell cycle arrest at the G1 phase.

Apoptosis Analysis

Cell Line:	MCF-7 and MCF-7/ADR cells[1]
Concentration:	2, 4 and 8 μM
Incubation Time:	48 hours
Result:	Induced apoptosis in a dose-dependent manner in MCF-7 cells, and increased the apoptotic rate of the cells from 2.8% to 15.2% in MCF-7/ADR.

Western Blot Analysis

Cell Line:	MCF-7[1]
Concentration:	1.5, 3 and 6 μM in MCF-7; 5, 10, and 20 μM in MCF-7/ADR
Incubation Time:	24 hours
Result:	Increased the expression degree of cleaved-caspase-3 and cleaved-PARP in MCF-7; down-regulated the level of anti-apoptotic protein bcl-2, up-regulated the levels of pro-apoptotic proteins bax and bad in MCF-7/ADR.

In Vivo

Topoisomerase I inhibitor 5 (1 mg/kg and 10 mg/kg; IV; every two days, for 21 days) decreases the tumor growth significantly [1].

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Animal Model:	Bal b/c nude mice (injected with 106 MCF-7 cells in the left flank for 7 days)[1]
Dosage:	1 mg/kg and 10 mg/kg
Administration:	IV; every two days, for 21 days
Result:	Decreased the tumor growth significantly and the tumor inhibition ratio reached to 32.4% at 1 mg/kg and 7.2% at 10 mg/kg.

REFERENCES

[1]. Zhong H, Zhao M, Wu C, Zhang J, Chen L, Sun J. Development of oxoisoaporphine derivatives with topoisomerase I inhibition and reversal of multidrug resistance in breast cancer MCF-7/ADR cells. Eur J Med Chem. 2022;235:114300.

Caution: Product has not been fully validated for medical applications. For research use only.

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