# Topo I/COX-2-IN-2

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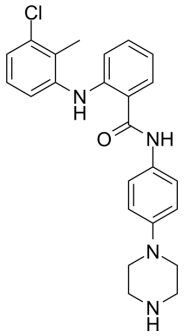
| **Cat. No.:** | HY-150755 |
| **CAS No.:** | 2841455-91-0 |
| **Molecular Formula:** | $C_{24}H_{25}ClN_4O$ |
| **Molecular Weight:** | 420.93 |
| **Target:** | Topoisomerase; COX; Apoptosis; Reactive Oxygen Species |
| **Pathway:** | Cell Cycle/DNA Damage; Immunology/Inflammation; Apoptosis; Metabolic Enzyme/Protease; NF-κB |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |



## BIOLOGICAL ACTIVITY

**Description**

Topo I/COX-2-IN-2 (Compound W10) is a potent dual-target inhibitor of Topo I and COX-2 with $IC_{50}$ values of 0.90 μM and 2.31 μM, respectively. Topo I/COX-2-IN-2 induces cancer cell apoptosis through the mitochondrial pathway[1].

**$IC_{50}$ & Target**

| Topoisomerase I | COX-2 |
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| 0.90 μM ($IC_{50}$) | 2.31 μM ($IC_{50}$) |

**In Vitro**

Topo I/COX-2-IN-2 (Compound W10) (0-30 μM) shows good toxicity against cancer cells[1].
Topo I/COX-2-IN-2 forms an ionic bonding interaction with DA13 of DNA to improve Topo I inhibition[1].
Topo I/COX-2-IN-2 (0-9 μM, 24 h) arrests cell cycle of HT29 and RKO at G1/G0 phase, induces apoptosis in HT29 and RKO cells through the mitochondrial pathway, and inhibits abnormal activation of the NF-κB/IκB pathway. [1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

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| Cell Line: | HT29, RKO, HCT116, LoVo and SW480 |
| Concentration: | 0-30 μM |
| Incubation Time: | 72 h |
| Result: | Showed good toxicity with $IC_{50}$ values of 1.48 ± 0.08 μM, 2.06 ± 0.01 μM, 4.89 ± 0.36 μM, 8.42 ± 0.22 μM and 7.36 ± 0.64 μM for HT29, RKO, HCT116, LoVo and SW480 cells, respectively. |

Cell Cycle Analysis[1]

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| Cell Line: | HT29 and RKO |
| Concentration: | 2, 4 and 8 μM for HT29; 3, 6 and 9 μM for RKO |
| Incubation Time: | 24 h |
| Result: | Blocked the cell cycle in G1/G0 phase in both HT29 and RKO. In HT29 cells, the arresting activity was not obvious for the ratio of G1/G0 phase in high-concentration treatment groupincreased from 55.20% to 65.17% slightly, while in RKO cells, the ratio of G1/G0 phase obviously increased from 37.57% to 76.99%. |

Apoptosis Analysis[1]

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| Cell Line: | HT29 and RKO |
| Concentration: | 2, 4 and 8 μM for HT29; 3, 6 and 9 μM for RKO |
| Incubation Time: | 24 h |
| Result: | Mainly induced the late apoptosis in HT29 cells and exhibited dual induction of lateand early apoptosis in RKO cells.<br>Induced the production of reactive oxygen species (ROS) burst and significantly reduce the mitochondrial membrane potential. |

Western Blot Analysis[1]

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| Cell Line: | HT29 and RKO |
| Concentration: | 2, 4 and 8 μM for HT29; 3, 6 and 9 μM for RKO |
| Incubation Time: | 24 h |
| Result: | Induced increased expression of the pro-apoptotic proteins Bax, cytochrome c and apoptotic effector cleaved caspase 3/9, reduced the expression of the inhibitory factor Bcl-2.<br>The expressions of phosphorylated NF-κB and IκB were significantly decreased. |

**In Vivo**

Topo I/COX-2-IN-2 (Compound W10) (15 and 30 mg/kg; i.p.; b.i.d for 2 weeks) inhibits tumor growth and shows obvious necrosis on tumor tissue[1].

Topo I/COX-2-IN-2 has acceptable pharmacokinetic properties for intraperitoneal injection and oral administration[1].

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

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| Animal Model: | Male BALB/c nude mice weighing 20–25 g, HT29 xenograft model[1] |
| Dosage: | 15 and 30 mg/kg |
| Administration: | Intraperitoneal injection, twice daily for 2 weeks |
| Result: | 30 mg/kg group immediately slowed down the tumor growth rate after administration, and almost completely prevented tumor growth in the later stage, and its tumor growth inhibition (TGI) was 57.86%. 15 mg/kg group showed 40.67% TGI.<br>Showed obvious necrosis on tumor tissue. |

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| Animal Model: | 250–280 g male SD rats[1] |
| Dosage: | 100 mg/kg and 30 mg/kg |
| Administration: | Intragastric administration (100 mg/kg) or intraperitoneal injection (30 mg/kg) (Pharmacokinetics Study) |
| Result: | Pharmacokinetic data of Topo I/COX-2-IN-2 (W10) in vivo[a][1] |

| Comp. | Dose (mg/kg) | Route | $T_{1/2}$(h) | $T_{max}$(h) | $C_{max}$ (μg/mL) | $AUC_{0-t}$ (μg⊠h/mL) |
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| Topo I/COX-2-IN-2 | 100 | p.o. | 8.87 ± 1.92 | 3.67 ± 0.58 | 2.00 ± 0.41 | 24.81 ± 5.76 |
| | 30 | i.p. | 4.27 ± 0.22 | 0.28 ± 0.05 | 1.60 ± 0.34 | 5.41 ± 0.20 |

[a] Topo I/COX-2-IN-2 was administered to 6 SD rats with different administration methods and doses, and the serum concentration was analyzed. The analysis method is the linear trapezoidal PKsolver 2.0 computer program of the non-compartmental model. All the data are from the above 6 rats, and the data are represented by the mean and standard deviation.

## REFERENCES

[1]. Hu X, et al. Discovery of dual inhibitors of topoisomerase I and Cyclooxygenase-2 for colon cancer therapy. Eur J Med Chem. 2022 Jun 23;240:114560.



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