# Topoisomerase I/II inhibitor 4

**Cat. No.:** HY-149002

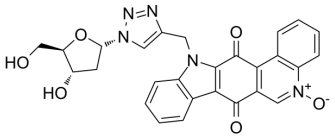
**Molecular Formula:** $C_{27}H_{21}N_5O_6$

**Molecular Weight:** 511.49

**Target:** Topoisomerase; 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/II inhibitor 4 (compound F16) is a potent topoisomerase I (Topo I) and II (Topo II) dual inhibitor. Topoisomerase I/II inhibitor 4 inhibits cell proliferation, invasion and migration and induces apoptosis. Topoisomerase I/II inhibitor 4 can be used for liver cancer research[1].

**In Vitro**

Topoisomerase I/II inhibitor 4 (compound F16) (0-100 μM) could intercalate into DNA to inhibit enzymatic activity and inhibit Topo I and II activities in a dose-dependent manner[1].

Topoisomerase I/II inhibitor 4 (compound F16) shows a high-expression level of Topo I and II enzymes in A375 and HCT116 cells and exhibits potent anti-proliferative activity with $IC_{50}$ values of 20 and 50 nM, respectively, 10-fold lower than L02[1].

Topoisomerase I/II inhibitor 4 (compound F16) (0-40 nM, A375 cell) inhibits cancer cell colony formation, invasion, migration and induces cell apoptosis[1].

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

Cell Cycle Analysis[1]

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|---|---|
| Cell Line: | A375 cells |
| Concentration: | 20, 40 and 80 nM |
| Incubation Time: | 24 hours |
| Result: | The cell cycle blocked at the S phase in a dose-dependent manner. |

Apoptosis Analysis[1]

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|---|---|
| Cell Line: | A375 cells |
| Concentration: | 40, 80 and 120 nM |
| Incubation Time: | 8, 16 and 24 hours |
| Result: | Induced apoptosis rates for 8, 16 and 24 h were 7.14, 23.78 and 36.21%, respectively. Induced apoptosis rates for 40, 80 and 120 nM were 23.26, 36.21 and 55.94%, respectively. |

Western Blot Analysis[1]

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|---|---|
| Cell Line: | A375 cells |

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|---|---|
| Concentration: | 40, 80 and 120 nM |
| Incubation Time: | 24 hours |
| Result: | The expression levels of Ccaspase-3, C-caspase-8, C-caspase-9, Bad and Bax increased in a dose-dependent manner, the Bcl-2 expression was obviously decreased. |

**In Vivo**

Topoisomerase I/II inhibitor 4 (compound F16) (10-50 mg/kg; i.v.; per 2 days, for 7 days) suppresses tumor growth in the A375 Xenograft Model[1].

Topoisomerase I/II inhibitor 4 (compound F16) of the plasma clearance rate (CL) was 7-fold lower than that of VP-16(0.007 L/min/kg). Topoisomerase I/II inhibitor 4 has a delayed elimination half-life of 151 min[1].

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

| | |
|---|---|
| Animal Model: | Female BALB/c nude mice (5–6 weeks)[1] |
| Dosage: | 10 and 20 mg/kg |
| Administration: | Intravenous injection; Per 2 days, for 14 days. |
| Result: | Inhibited tumor growth in a melanoma xenograft mouse model and no apparent loss in body weight. |

| | |
|---|---|
| Animal Model: | Kunming male mice [1] |
| Dosage: | 10 mg/kg |
| Administration: | Intravenous injection; for 5 , 15 , 30 , 60 , 120 , 240 and 360 min. |

Result:

| Parameter | F16 | VP-16 |
|---|---|---|
| Dose (i.v.) mg/kg | 10 | 10 |
| $C_{max}$ (ng/mL) | 26952 | 17712 |
| $T_{max}$ (min) | 5 | 5 |
| $AUC_{plasma}$ (min*ng/mL) | 2878363 | 409528 |
| $T_{1/2}$ (min) | 151 | 45 |
| Vd (L/Kg) | 0.2341 | 0.432 |
| CL (L/min/kg) | 0.001 | 0.007 |

## REFERENCES

[1]. Yang X, et al. Optimization of the Natural Product Calothrixin A to Discover Novel Dual Topoisomerase I and II Inhibitors with Improved Anticancer Activity. J Med Chem.

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