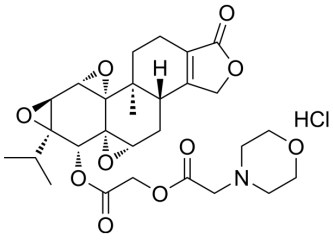
Antitumor agent-76

Cat. No.:	HY-151404
CAS No.:	2787593-12-6
Molecular Formula:	$C_{28}H_{36}ClNO_{10}$
Molecular Weight:	582.04
Target:	Apoptosis
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Antitumor agent-76 (Compound TP-P1) is an orally active, rapid-release and water-soluble Triptolide (HY-32735) proagent with antitumor activity[1].

In Vitro

Antitumor agent-76 (Compound TP-P1) shows good stability in aqueous solution, and the aqueous solubility (6.13 mg/mL in water) improved significantly compared to Triptolide[1].

Antitumor agent-76 (50 μg/mL) can be rapidly and completely converted into Triptolide within 30 min in rat plasma and within 45 min in human plasma. The concentration of Antitumor agent-76 has no significant effect on conversion rate[1].

Antitumor agent-76 (30-120 nM; 24 h) shows antiproliferative activities against acute myeloid leukemia (AML) cells without cytotoxicity towards normal cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	THP-1 and MV-4-11 cells
Concentration:	30, 60, or 120 nM
Incubation Time:	24 h
Result:	Showed antiproliferative activities with IC_{50}s of 14.79±0.42 nM and 45.97±0.13 nM against THP-1 and MV-4-11 cells, respectively.

In Vivo

Antitumor agent-76 (Compound TP-P1) (0-1.2 mg/kg; i.p.; daily for 28 days) inhibits tumor cell growth, proliferation and induces tumor cell apoptosis in mouse THP-1 and MV-4-11 xenografts models[1].

Antitumor agent-76 (100, 300 μg/kg/day; i.g.; 11 days) dose-dependently inhibits tumor growth in mouse MV-4-11 xenograft models[1].

Antitumor agent-76 is easily hydrolyzed in liver microsomes due to the high content of esterase in liver. The half-life is short ($T_{1/2}$=8.64 min) and the clearance rate is high[1].

Pharmacokinetic study of Antitumor agent-76 (Compound TP-P1) and triptolide on Sprague Dawley rats[a][1].

a

b

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

The values presented are the mean values from three independent mice. Dosed po (oral administration) was administered via oral gavage.

Compd	dosage[b] (mg/kg)	$AUC_{(0-t)}$ (h ng/ml)	T_{max} (h)	$V_{Z/F}$ (L/kg)	$CL_{Z/F}$ (L/h/kg)	C_{max} (μg/L)
Antitumor agent-76	1.6	60.46	0.50	37831.99	24563.25	23.53

Animal Model:	Male BALB/c Nude mice, THP-1 xenograft and MV-4-11 xenograft[1]
Dosage:	0.1, 0.3, 0.6, 1.2 mg/kg for THP-1 xenograft, 25, 50, 100 μg/kg for MV-4-11 xenograft
Administration:	Intraperitoneal administration, daily for 28 days
Result:	Significantly and dose-dependently inhibited the tumor growth in THP-1 xenografts, with an excellent tumor growth inhibitory rate (TGI) of 93.87% at the dosage of 100 μg/kg. Inhibited cell proliferation and induced cell apoptosis in tumor tissues. Also showed excellent antitumor activity in MV-4-11 xenograft models (25 μg/kg with a TGI of 54.3%), and the tumors achieved complete regression on day 12 at the dosage of 100 μg/kg.

Animal Model:	Sprague Dawley rats[1]
Dosage:	1.6 mg/kg
Administration:	Oral administration (Pharmacokinetic Analysis)
Result:	Exhibited an acceptable pharmacokinetic property.

REFERENCES

[1]. Kang D, et al. Discovery of a novel water-soluble, rapid-release triptolide prodrug with improved drug-like properties and high efficacy in human acute myeloid leukemia. Eur J Med Chem. 2022 Sep 5;243:114694.

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