Triptolide

Cat. No.: HY-32735

CAS No.: 38748-32-2

Molecular Formula: $C_{20}H_{24}O_6$

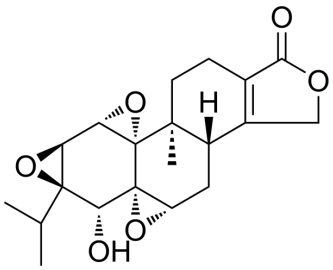
Molecular Weight: 360

Target: NF-κB; Apoptosis

Pathway: NF-κB; Apoptosis

Storage: 4°C, stored under nitrogen

* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (69.44 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7778 mL	13.8889 mL	27.7778 mL
5 mM	0.5556 mL	2.7778 mL	5.5556 mL
10 mM	0.2778 mL	1.3889 mL	2.7778 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.17 mg/mL (3.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.17 mg/mL (3.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Triptolide is a diterpenoid triepoxide extracted from the root of Tripterygium wilfordii with immunosuppressive, anti-inflammatory, antiproliferative and antitumour effects. Triptolide is a NF-κB activation inhibitor[1][2][3][4][5][6].

IC_{50} & Target

HSP90

MDM-2/p53
47-73 nM (IC_{50})

In Vitro

Triptolide induces apoptosis in cultured and primary Chronic Lymphocytic Leukemia (CLL) B-cells. Treatment of $CD19^+$ B cells with Triptolide, induces a dose-dependent increase in apoptosis in cultured and primary CLL cells. Triptolide is selectively toxic to both high risk (n=5) and low risk CLL (n=12) B cells (10 to 50 nM range) while largely sparing normal B-cells (n=5). Consistent with the inhibition of heat-shock induced HSP transcription, treatment with Triptolide attenuates

heat-shock induced expression of HSPs[1]. Triptolide is a natural product derived from the Chinese plant Tripterygium wilfordii, is reported to exhibit antitumor effects in a broad range of cancers. Triptolide inhibits MDM2 expression in a dose-dependent manner, even at low concentrations spanning 20-100 nM in acute lymphoblastic leukemia (ALL) cells. Triptolide exhibits strongly cytotoxic activity in all 8 cell lines having native MDM2 overexpression, with IC_{50} values range from 47 to 73 nM. Triptolide exhibits much less cytotoxic effect on EU-4 cells that express very low level of MDM2, while it effectively kill these cells when MDM2 is stably transfected (IC_{50} values: 725 nM vs. 88 nM)[2]. Differentiated PC12 cells are incubated with different concentrations of Triptolide (0.01, 0.1, and 1 nM) in the presence of 10 μM $A\beta_{25-35}$ for 24 hours and MTT assay is used to detect the effect of Triptolide. The results show that $A\beta_{25-35}$ can decrease the cell viability and when treated with Triptolide the viability of differentiated PC12 cells is significantly increased. The results indicate that Triptolide can alleviate cellular damage caused by $A\beta_{25-35}$, which means that Triptolide has a neuroprotective effect[3].

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

In Vivo

The Triptolide (TP) plasma concentrations are declined rapidly in mice after receive an intravenous dose. After 2h of injection, the Triptolide concentrations are dropped below the lower limit of quantification for all three groups. A comparison of the parameters is made between the control and the treated groups to assess the effect of P-gp inhibition on the Triptolide exposure and elimination. Treatment with the mdr1a-siRNA can significantly enhance the Triptolide plasma exposure, with the C_{max} increases from 413±74 to 510±94 ng/mL ($P<0.05$) and the AUC from 103.5±9.6 to 154.3±30.2 ng h/mL ($P<0.05$). In the concomitant group with Tariquidar, the significantly increased AUC is also noted, from 103.5±9.6 of the control to 145.9±24.6 ng h/mL of the Triptolide+Tariquidar group ($P<0.05$). Accordingly, the total body clearance of Triptolide in mice is remarkably decreased, from 9564±1024.2 mL/min/kg of the control to 6576.4±1438.5 ($P<0.05$) and 5755.4±1200.1 mL/min/kg ($P<0.05$) for Triptolide+Tariquidar and Triptolide+mdr1a-siRNA groups, respectively[4].

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

PROTOCOL

Cell Assay [3]

The viability of differentiated PC12 cells treated with different concentrations of Triptolide. After differentiated PC12 cells are cultured on 96-well plates with RPMI 1640 medium for stabilization, differentiated PC12 cells are incubated with different concentrations of Triptolide (0.01, 0.1, and 1 nM) for 24 hours. The concentrations in this study are chosen. Then cell viability is determined by the MTT assay. Each condition and experiment is repeated three times[3].

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

Animal Administration [4]

Mice[4]

Male BALB/C mice (weight, 18-22 g) are used. For Triptolide (TP) plasma kinetic study and toxicological evaluation, mice are divided into four groups (n=5 each) to collect blood and tissue samples: (1) normal+saline group; (2) 1.0 mg/kg Triptolide+15 nmol negative control (NC) siRNA-siRNA group; (3) 1.0 mg/kg Triptolide+15 nmol mdr1a-siRNA group; (4) 1.0 mg/kg Triptolide+10 mg/kg Tariquidar group. In order to avoid the complication caused by drug absorption or possible intestinal first-pass effect, Triptolide and the inhibitor are intravenously administrated to mice. The siRNA group is intravenously injected with NC-siRNA or mdr1a-siRNA 2 days before Triptolide dose. For Triptolide+Tariquidar group, the mice are received an intravenous Tariquidar dose 20 min prior to the Triptolide injection. Blood samples are collected at 2, 5, 10, 15, 30, 60 and 120 min after Triptolide dosing. To assess the liver exposure of Triptolide, liver tissue samples are collected from another set of mice at 5, 30, 60 and 120 min after dosing. Three Triptolide groups are design for this experiment, including Triptolide+NC-siRNA group, Triptolide+mdr1a-siRNA group and Triptolide+Tariquidar group. The liver tissue samples are weighed and then homogenized in 10 volume (w:v) of ice-cold saline. The concentrations of Triptolide in plasma and liver tissue are measured by a validated LC-MS/MS method.

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

CUSTOMER VALIDATION

- Blood. 2020 Jul 23;136(4):501-515.

- Nucleic Acids Res. 2020 Dec 16;48(22):e127.
- Clin Cancer Res. 2020 Apr 15;26(8):2011-2021.
- Proc Natl Acad Sci U S A. 2023 May 23;120(21):e2303698120.
- Proc Natl Acad Sci U S A. 2020 May 5;117(18):9964-9972.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Ganguly S, et al. Targeting HSF1 disrupts HSP90 chaperone function in chronic lymphocytic leukemia. Oncotarget. 2015 Oct 13;6(31):31767-79.

[2]. Huang M, et al. Triptolide inhibits MDM2 and induces apoptosis in acute lymphoblastic leukemia cells through a p53-independent pathway. Mol Cancer Ther. 2013 Feb;12(2):184-94.

[3]. Xu P, et al. Triptolide Inhibited Cytotoxicity of Differentiated PC12 Cells Induced by Amyloid-Beta25-35 via the Autophagy Pathway.PLoS One. 2015 Nov 10;10(11):e0142719.

[4]. Kong LL, et al. Inhibition of P-glycoprotein Gene Expression and Function Enhances Triptolide-induced Hepatotoxicity in Mice.Sci Rep. 2015 Jul 2;5:11747.

[5]. Zhang W, et al. Triptolide Combined with Radiotherapy for the Treatment of Nasopharyngeal Carcinoma via NF-κB-Related Mechanism. Int J Mol Sci. 2016 Dec 19;17(12). pii: E2139.

[6]. Cai J, et al. Natural product triptolide induces GSDME-mediated pyroptosis in head and neck cancer through suppressing mitochondrial hexokinase-II. J Exp Clin Cancer Res. 2021;40(1):190. Published 2021 Jun 9.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA