Tilorone dihydrochloride

Cat. No.: HY-B1080

CAS No.: 27591-69-1

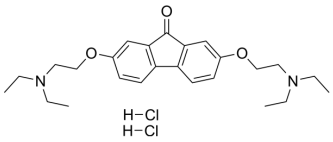
Molecular Formula: $C_{25}H_{36}Cl_2N_2O_3$

Molecular Weight: 483.47

Target: HIF/HIF Prolyl-Hydroxylase; Influenza Virus

Pathway: Metabolic Enzyme/Protease; Anti-infection

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 1 year; -20°C, 6 months (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (206.84 mM; Need ultrasonic)
DMSO : 12.5 mg/mL (25.85 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0684 mL	10.3419 mL	20.6838 mL
5 mM	0.4137 mL	2.0684 mL	4.1368 mL
10 mM	0.2068 mL	1.0342 mL	2.0684 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 25 mg/mL (51.71 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (2.59 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tilorone dihydrochloride is an orally active interferon (IFN) inducer with broad-spectrum antiviral activities. Tilorone dihydrochloride possesses robust anti-Severe fever with thrombocytopenia syndrome virus (SFTSV) activity in vitro and in vivo through stimulation of host innate immunity. Tilorone dihydrochloride can penetrate the blood-brain barrier to activate HIF in the CNS[1][2][3].Tilorone dihydrochloride exhibits an inhibitory activity with EC_{50} of 230 nM against Ebola virus (EBOV)[4].

In Vitro

Tilorone (0.1, 0.3, 1 μM) dihydrochloride inhibits SFTSV-induced cytopathological effect (CPE) in a dose-dependent manner with no cell toxicity in Huh7 cells[1].

Tilorone dihydrochloride reveals drug-like properties, with solubility of 465 μM at pH 7.4, stable mouse microsomal metability (half-time: 47.8 min; CL: 14.5 μL/min/mg) and Caco-2 permeability (10 μM) of 20.4×10^{-6} cm/s and 8.87×10^{-6} cm/s [4].

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

In Vivo

Tilorone (5-20 mg/kg; intraperitoneally; once daily at 1-7 days) dihydrochloride with 20 mg/kg protects 78.94% of the mice from lethal challenge with virus intracranially[1].

Tilorone (5, 10 mg/kg; intraperitoneally; 12 h prior to challenge, at the time point of challenge, and 12 h after challenge) dihydrochloride with 10 mg/kg dose-dependently inhibits viremia, causes a general increase in IFN-α and IFN-β, reduces the TNF-α and IL-10 in a viremia model based on wild-type 6-week-old female BALB/c mice with SFTSV[1].

Tilorone dihydrochloride (10-50 mg/kg, i.p., once daily for 8 days) exhibits a dose-efficient range against EBOV of 25-50 mg/kg, with full clearance of virus in mice[4].

Tilorone dihydrochloride (30-60 mg/kg, i.p., once, 2 h , 24 h and 48 h postinfection) reveals 100% survival rate at dosage of 30 mg/kg in BALB/c mice, when dosed at 2 h and 24 h postinfection[4].Tilorone dihydrochloride (2-10 mg/kg, once, i.p.) reveals a pharmacokinetic parameter in BLAB/c mice [4]:

Pharmacokinetic Analysis of Tilorone in BALB/c mice[1]

Dose (mg/kg)	Sex	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/ml)	AUC_{last} (ng·h/ml)	AUC_{inf} (ng·h/ml)	CL_{blood} (ml/h/kg)	V (ml/kg)
2	M	15.7	0.083	50.5	356	516	87900	3870
2	F	18.7	0.083	17.5	133	210	257000	9510
10	M	20.8	0.25	135	1099	1940	155000	5160
10	F	18.9	0.25	92.3	513	793	343000	12600

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Animal Model:	Wild-type 1-day-old suckling ICR mice with ethal virus challenge model[1]
Dosage:	5, 10, 20 mg/kg
Administration:	Intraperitoneally; once daily at 1-7 days
Result:	Protected 78.94% of the mice from lethal challenge, compared with none in the vehicle group at 21 days post infection.

Animal Model:	EBOV in BLAB/c mice[4]
Dosage:	30-60 mg/kg
Administration:	Intraperitoneal injection, signle dosage: 2 h, 24 h and 48 h postinfection
Result:	Exhibited 100% survival rates at 2 h and 24 h postinfection, with dosage of 30 mg/kg.

CUSTOMER VALIDATION

- Biomed J. 2020 Aug;43(4):368-374.

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REFERENCES

[1]. Jingjing Yang, et al. Tilorone confers robust in vitro and in vivo antiviral effects against severe fever with thrombocytopenia syndrome virus. Virol Sin. 2022 Feb;37(1):145-148.

[2]. Sean Ekins, et al. Tilorone, a Broad-Spectrum Antiviral for Emerging Viruses. Antimicrob Agents Chemother. 2020 Apr 21;64(5):e00440-20.

[3]. Rajiv R Ratan, et al. Small molecule activation of adaptive gene expression: tilorone or its analogs are novel potent activators of hypoxia inducible factor-1 that provide prophylaxis against stroke and spinal cord injury. Ann N Y Acad Sci. 2008 Dec:1147:383-94.

[4]. Ekins S, et al., Efficacy of Tilorone Dihydrochloride against Ebola Virus Infection. Antimicrob Agents Chemother. 2018 Jan 25;62(2):e01711-17.

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