Zotatifin

Cat. No.: HY-112163

CAS No.: 2098191-53-6

Molecular Formula: $C_{28}H_{29}N_3O_5$

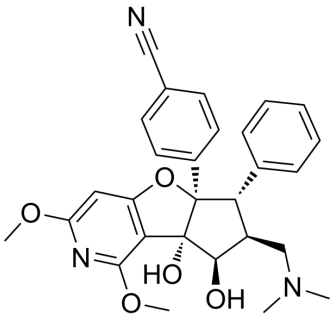
Molecular Weight: 487.55

Target: Eukaryotic Initiation Factor (eIF); Apoptosis; SARS-CoV

Pathway: Cell Cycle/DNA Damage; Apoptosis; Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 200 mg/mL (410.21 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0511 mL	10.2554 mL	20.5107 mL
5 mM	0.4102 mL	2.0511 mL	4.1021 mL
10 mM	0.2051 mL	1.0255 mL	2.0511 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5 mg/mL (10.26 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (10.26 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zotatifin (eFT226) is a potent, selective, and well-tolerated eIF4A inhibitor. Zotatifin promotes eIF4A binding to specific mRNA sequences with recognition motifs in the 5'-UTRs (IC_{50}=2 nM) and interferes with the assembly of the eIF4F initiation complex[1]. Zotatifin shows robust antiviral effects, it effectively reduces viral infectivity by inhibiting SARS-CoV-2 NP protein biogenesis (IC_{90}=37 nM)[2]. Zotatifin induces cell apoptosis[1].

IC_{50} & Target

eIF4

In Vitro

Zotatifin induces the formation of a stable ternary complex [eIF4A-RNA-eFT226]. Zotatifin increases the residence time for eIF4A1 binds to an AGAGAG RNA surface, the K_d values are 0.021 μM and 8.0 μM, respectively for eFT226 presence or absence [1].

Zotatifin inhibits in vitro translation as a sequence-dependent manner, the IC_{50} values are 1.5 nM, 13.8 nM, 92.5 nM, and 217.5 nM, respectively in an MDA-MB-231 cell line with transiently transfected AGAGAG, GGCGGC, CCGCCG and CAACAA 5'-UTRs-containing sequences[1].

Zotatifin (0.0001 μM-1 μM; 72 hours) inhibits tumor cells growth as a dose-dependent manner. It shows a potent anti-proliferative activity (GI_{50}<15 nM) in MDA-MB-231 tumor cells, but eIF4A1 F163L mutation rescues eFT226 anti-proliferative activity[1].

Zotatifin (0.0001 μM-1 μM; 72 hours) inhibits tumor cell growth, exhibits GI_{50} values for TMD8, SU-DHL-2, HBL1, Pfeiffer, SU-DHL-6, SU-DHL-10, VAL, Carnaval, U2973, Ramos, Jeko1, Mino, and Rec-1 cells are 4.1 nM, 3 nM, 5.6 nM, 3.7 nM, 5.3 nM, 7.3 nM, 6.6 nM, 4.4 nM, 4.2 nM, 4.6 nM, 7.9 nM, 11.2 nM and 11.8 nM, respectively[1].

Zotatifin (30 μM-100 μM; 3 or 24 hours) results in translational regulation of oncogenic protein, decreases MYC,CCND3,BCL2 and MCL1 protein expression as a time- and dose-dependent manner[1].

The anti-viral activity of Zotatifin is demonstrated by various assays: such as TCID50 assay, Plaque assay, NP-staining assay, et al[2].

Zotatifin (10 nM, 100 nM, 200 nM, 500 nM, 2 μM, 10 μM; 1 or 2 hours pre-treatment before virus isolates) decreases the detection of the viral NP protein and reduces viral infectivity in a concentration-dependent matter in Vero E6 cells cells infected with SARS-CoV-2 isolates[2].

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

Cell Viability Assay[1]

Cell Line:	MDA-MB-231 tumor cells
Concentration:	0.0001 μM, 0.001 μM, 0.01 μM, 0.1 μM, 1 μM
Incubation Time:	72 hours
Result:	Inhibited cell growth with a GI_{50} of 15 nM, and F163L mutant rescued anti-proliferative effects.

Cell Proliferation Assay[1]

Cell Line:	DLBCL-ABC; DLBCL-GCB; Burkitt; and MCL tumor type cells
Concentration:	0.0001 μM, 0.001 μM, 0.01 μM, 0.1 μM, 1 μM
Incubation Time:	72 hours
Result:	Inhibited cell growth with GI_{50} values ranging from 3 nM to 20 nM.

Cell Proliferation Assay[1]

Cell Line:	TMD8 and Pfeiffer DLBCL tumor cells
Concentration:	30 μM; 100 μM
Incubation Time:	3 or 24 hours
Result:	Decreased MYC, CCND3, Bcl2,and MCL1 protein levels.

In Vivo

Zotatifin (intravenous injection; 1 mg/kg; 14-22 days) decreases tumor volume, inhibits the TMD8 xenograft-bearing, HBL1 xenograft-bearing, Pfeiffer xenograft-bearing, SU-DHL-6 xenograft-bearing, SU-DHL-10 xenograft-bearing and Ramos-bearing animals'tumor growth as percentage of 97%, 87%, 70%, 83%, 37% and 75%, respectively[1].

Zotatifin (intravenous injection; 0.001 mg/kg-1 mg/kg; 15 days) inhibits the growth of B-cell lymphoma xenografts and is well-tolerated against B-cell lymphoma xenograft models in vivo[1].

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

Animal Model:	B-cell lymphoma xenograft model[1]
Dosage:	0.001 mg/kg; 0.1 mg/kg; 1 mg/kg
Administration:	Intravenous injection; 15 days
Result:	Showed efficacy in B-cell lymphoma xenograft models.

CUSTOMER VALIDATION

- J Clin Invest. 2023 Jun 29;e167651.
- Cell Rep. 2021 Oct 12;37(2):109806.
- Int J Mol Sci. 2023, 24(3), 2055.
- Viruses. 2022, 14(3), 519.
- Pharmaceuticals. 2022, 15(9), 1086.

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REFERENCES

[1]. Peggy A. Thompson, et al. Preclinical Evaluation of eFT226, a Novel, Potent and Selective eIF4A Inhibitor with Anti-tumor Activity in B-cell Malignancies.

[2]. Gordon DE, et al. A SARS-CoV-2 protein interaction map reveals targets for drug repurposing.Nature. 2020 Apr 30.

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