RIP1/RIP3/MLKL activator 1

Cat. No.: HY-144828

CAS No.: 2682850-41-3

Molecular Formula: $C_{43}H_{56}N_4O_3$

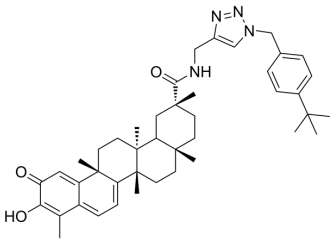
Molecular Weight: 676.93

Target: RIP kinase; Mixed Lineage Kinase; Necroptosis

Pathway: Apoptosis; MAPK/ERK Pathway

Storage: 4°C, stored under nitrogen

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (147.73 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4773 mL	7.3863 mL	14.7726 mL
	5 mM	0.2955 mL	1.4773 mL	2.9545 mL
	10 mM	0.1477 mL	0.7386 mL	1.4773 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: ≥ 2.5 mg/mL (3.69 mM); Suspended solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (3.69 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

RIP1/RIP3/MLKL activator 1 (Compound 6i) is a potent anti-glioma agent. RIP1/RIP3/MLKL activator 1 induces necroptosis through RIP1/RIP3/MLKL pathway. RIP1/RIP3/MLKL activator 1 exerts acceptable BBB permeability[1].

IC_{50} & Target

RIP1, RIP3, MLKL[1]

In Vitro

RIP1/RIP3/MLKL activator 1 (Compound 6i) (96 h) shows antiproliferative activities in human glioma cell lines[1].
RIP1/RIP3/MLKL activator 1 (0-4 μM, 0-72 h) exhibits remarkable antiproliferative activity for U251 cells in a time- and concentration-dependent manner[1].
RIP1/RIP3/MLKL activator 1 (10 μM, 0-72 h) shows acceptable stability[1].
RIP1/RIP3/MLKL activator 1 (0-2 μM, 24 h) effectively inhibits the migration of U251 cells[1].
RIP1/RIP3/MLKL activator 1 induces necroptosis through RIP1/RIP3/MLKL pathway, and induces mitochondrial

depolarization in U251 cells[1].
RIP1/RIP3/MLKL activator 1 could not induce apoptosis in U251 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	A172, LN229, U87, U251 and L02 cell lines
Concentration:	0-4 μM for U251 cells
Incubation Time:	96 h; 24, 48, and 72 h for U251 cells
Result:	Showed antiproliferative activity with IC_{50} values of 3.03 ± 0.70, 1.78 ± 0.79, 1.22 ± 0.89, 0.94 ± 0.45, and 0.99 ± 0.46 μM against A172, LN229, U87, U251 and L02 cells, respectively. Time- and concentration-dependently inhibited the growth in U251 cells.

Western Blot Analysis[1]

Cell Line:	U251
Concentration:	0, 0.5, 1, 2, and 4 μM
Incubation Time:	24 or 48 h
Result:	Concentration-dependently upregulated the expression of p-RIP1, RIP1, p-RIP3, RIP3, p-MLKL, and MLKL at 24 or 48 h.

In Vivo

RIP1/RIP3/MLKL activator 1 (Compound 6i) (2.50 ng/tail; i.v.; 48 h) inhibits U251 cell proliferation in vivo and exerts acceptable BBB permeability[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Zebrafish wide-type AB strain; 200 CM-DiI labeled U251 cells were transplanted into yolk sac of each wild-type zebrafish embryos at 2 dpf (2 days postfertilization)[1]
Dosage:	2.50 ng/tail
Administration:	Microinjection; 48 h
Result:	Remarkably reduced the U251 xenografts fluorescence intensity.

REFERENCES

[1]. Yao Feng, et al. Synthesis and biological evaluation of celastrol derivatives as potential anti-glioma agents by activating RIP1/RIP3/MLKL pathway to induce necroptosis. Eur J Med Chem. 2022 Feb 5;229:114070.

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