SZM679

Cat. No.: HY-151873

Molecular Formula: $C_{27}H_{18}F_5N_3O_5S$

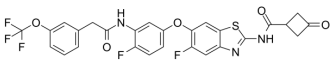
Molecular Weight: 591.51

Target: RIP kinase

Pathway: Apoptosis

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (211.32 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6906 mL	8.4529 mL	16.9059 mL
	5 mM	0.3381 mL	1.6906 mL	3.3812 mL
	10 mM	0.1691 mL	0.8453 mL	1.6906 mL

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

BIOLOGICAL ACTIVITY

Description

SZM679 is a potent, orally active and selective RIPK1 inhibitor with K_d values of 8.6 nM and >5000 nM for RIPK1 and RIPK3, respectively. SZM679 reverses the tumor necrosis factor-induced systemic inflammatory response. SZM679 decreases the Tau hyperphosphorylation, neuroinflammation, and the RIPK1 phosphorylation level in the hippocampus and cortex. SZM679 can be used in research of Alzheimer's disease (AD)[1].

IC_{50} & Target

RIPK1	RIPK3
8.6 nM (Kd)	>5000 nM (Kd)

In Vitro

SZM679 (0-10 μM; 24 h; necrotic L929 and HT-29 cells) has an anti-necrosis activity by Inhibiting the RIPK1 pathway with an EC_{50} value of 2 nM. SZM679 also protects against TNF-α, cycloheximide, and z-VAD-fmk (TCZ)-induced necroptosis. SZM679 protects against necroptosis induced by TZ in a dose dependent manner[1].

SZM679 (1 μM; 6 h; necrotic HT-29 cells) selectively inhibits the expression of RIPK1 but not RIPK3 or MLKL. SZM679 blocks necrosome formation by inhibiting TSZ-induced phosphorylation of RIPK1[1].

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

Western Blot Analysis[1]

Cell Line:	Necrotic HT-29 cells
Concentration:	1 μM
Incubation Time:	6 hours
Result:	Inhibited the phosphorylation of RIPK1 at 1 μM, resulting in the inhibition of the downstream phosphorylation of RIPK3 and MLKL.

In Vivo

SZM679 (10-40 mg/kg; i.p.; male C57BL/6 J mice with TNF-induced SIRS models) protects against necroptosis-specific TNF-induced systemic inflammatory response syndrome (SIRS) in vivo[1].

SZM679 (1 mg/kg; administered intragastrically; once daily for 7 days) improves cognitive function in STZ-induced AD mice [1].

SZM679 (1 mg/kg; administered intragastrically; once daily for 7 days) rescues brain structure damage with no obvious toxicity and decreases AD biomarkers and decreases the expression levels of inflammatory cytokines and inhibits RIPK1 phosphorylation in the brain tissues of AD mice[1].

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

Animal Model:	Male C57BL/6 J mice with TNF-induced SIRS models[1]
Dosage:	10, 20, and 40 mg/kg
Administration:	Intraperitoneal injection
Result:	Protected mice in a dose-dependent manner from hypothermia and death.

Animal Model:	Male C57BL/6 J mice with AD models[1]
Dosage:	1 mg/kg
Administration:	Administered intragastrically; once daily for 7 days
Result:	Improved the anxiety, behavior, and exploratory ability of AD mice. Improved the learning and memory ability of AD mice.

Animal Model:	Male C57BL/6 J mice with AD models[1]
Dosage:	1 mg/kg
Administration:	Administered intragastrically; once daily for 7 days
Result:	Rescued the damaged hippocampal structure of AD mice and restored the cell number and morphology. Down-regulated the expression of the inflammatory cytokines, the IL-1β and TNF-α levels.

REFERENCES

[1]. Sun Y, et, al. Discovery of a Trifluoromethoxy Cyclopentanone Benzothiazole Receptor-Interacting Protein Kinase 1 Inhibitor as the Treatment for Alzheimer's Disease. J Med Chem. 2022 Nov 10;65(21):14957-14969.

Caution: Product has not been fully validated for medical applications. For research use only.

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