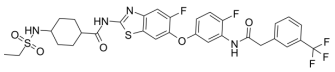
SZM-1209

Cat. No.:	HY-149052
CAS No.:	2919801-86-6
Molecular Formula:	$C_{31}H_{29}F_5N_4O_5S_2$
Molecular Weight:	696.71
Target:	RIP kinase; Mixed Lineage Kinase; Necroptosis
Pathway:	Apoptosis; MAPK/ERK Pathway
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

SZM-1209 is an orally active, potent and specific RIPK1 inhibitor, with a K_d of 85 nM. SZM-1209 exhibits high anti-necroptotic activity (EC_{50}=22.4 ± 8.1 nM). SZM-1209 shows anti-SIRS (systemic inflammatory response syndrome), and anti-ALI (acute lung injury) effects[1].

IC_{50} & Target

RIPK1	RIPK3
85 nM (Kd)	>10000 nM (Kd)

In Vitro

SZM-1209 blocks necroptosis in a dose-dependent manner[1].

SZM-1209 (0-1 μM, 6 h) specifically inhibits phosphorylation of RIPK1-RIPK3-MLKL necroptosis signaling[1].

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

Western Blot Analysis[1]

Cell Line:	HT-29 cells
Concentration:	0.1, 0.5, and 1 μM
Incubation Time:	6 h
Result:	SZM-1209 at 1 μM completely inhibited phosphorylation of both RIPK1 and RIPK3 in 2-6 h, and subsequently inhibited the phosphorylation of downstream MLKL.

In Vivo

SZM-1209 (25-100 mg/kg, IG) can reverse mouse deaths with significant anti-inflammatory effects in a mTNF-α-induced systemic inflammatory response syndrome (SIRS) model[1].

SZM-1209 (25-100 mg/kg, IP) significantly alleviates ALI (acute lung injury) by reducing pulmonary edema and pathological damage[1].

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

Animal Model:	C57BL/6J mice (female, 6-8 weeks old, mTNF-α (intravenous injection)-induced SIRS model)[1]
Dosage:	25, 50, and 100 mg/kg
Administration:	Intragastric administration

Result:	Dose-dependently improved survival rates of the SIRS mice to 30, 90, and 100%. Could effectively protect against mTNFα-induced SIRS in vivo. Serum levels of IL-6 and IL-1β were significantly decreased.

Animal Model:	C57BL/6J mice (female, 6-8 weeks old, NNK (HY-126477) (65 mg/kg) short-term intratracheal exposure-induced ALI model)[1]
Dosage:	25, 50, and 100 mg/kg
Administration:	IP
Result:	Exhibited lower levels of IL-6 and TNF-α in BALF than those of model mice. Inhibited the expression of inflammatory genes of IL-6 and TNF-α in lung tissues of mice at a mRNA level. Significant reduced phosphorylation of RIPK1, and also completely blocked at a high dose of 100 mg/kg in lung tissue of ALI model mice.

REFERENCES

[1]. Zhang X, et al. Targeting Receptor-Interacting Protein Kinase 1 by Novel Benzothiazole Derivatives: Treatment of Acute Lung Injury through the Necroptosis Pathway. J Med Chem. 2023 Apr 13;66(7):5261-5278.

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