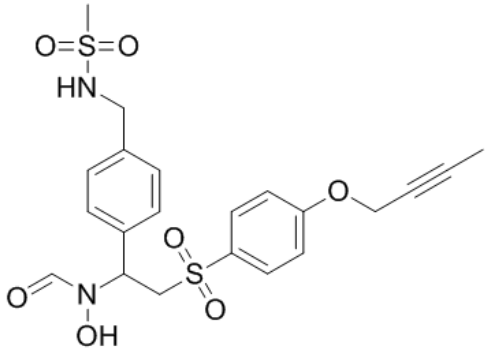
Product Data Sheet

Product Name: KP-457
Cat. No.: GC32452

Chemical Properties

Cas. No.	1365803-52-6		
SMILES	CS(=O)(NCC1=CC=C(C(N(C=O)O)CS(=O)(C2=CC=C(OCC#CC)C=C2)=O)C=C1)=O		
Formula	$C_{21}H_{24}N_2O_7S_2$	M.Wt	480.55
Solubility	DMSO : 125 mg/mL (260.12 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:	
Cell lines	RBL-2H3 cells (rat basophilic leukemia cell line, tumor analog of mucosal mast cells)

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Preparation Method	RBL-2H3 cells were maintained in DMEM complete medium containing 4.5g/L D-Glucose, 110mg/L sodium pyruvate, 1x Glutamax, and 10% heat-inactivated FBS at 37°C and 5% CO_2. Cells were sensitized with 0.5μg/mL mouse anti-TNP IgE for 3 hours, then stimulated with 25ng/mL TNP(26)-BSA along with specified amounts of KP-457 (0.3μM, 1μM, 3μM, or 10μM) or solvent DMSO for 1 hour. After stimulation, β-hexosaminidase activities and TNF levels in the supernatant and cell lysates were quantified.
Reaction Conditions	0.3-10μM; 1h
Applications	KP-457 did not affect the exocytosis of β-hexosaminidase. KP-457 significantly reduced the amount of soluble TNF protein released into the supernatant. KP-457 inhibited the overall level of total TNF in allergen-triggered RBL-2H3 cells.

References:

[1] Ayo TE, Adhikari P, Xu H. TNFR1 Links TNF Exocytosis to TNF Production in Allergen-Activated RBL-2H3 Cells. Cell Signal. 2023 May;105:110607.

Background

KP-457 is a selective inhibitor of A disintegrin and metalloproteinase 17 (ADAM17) with an IC_{50} of 11.1nM. KP-457 inhibits ADAM10 (IC_{50}=748nM), MMP2 (IC_{50}=717nM), MMP3 (IC_{50}=9760nM), MMP7 (IC_{50}=2200nM), MMP9 (IC_{50}=5410nM), MMP13 (IC_{50}=930nM), MMP14 (IC_{50}=2140nM), and MMP17 (IC_{50}=7100nM). KP-457 blocks Zn^{2+} chelation in the catalytic domain of ADAM17, inhibits GPIbα shedding, and effectively enhances the production of functional iPSC-derived platelets. KP-457 can be used for research related to protease/MMP pathways and iPSC-derived platelets[1-4].

In vitro, co-treatment of anti-TNP IgE-sensitized RBL-2H3 cells with 0.3-10μM KP-457 and TNP(26)-BSA for 1 hour significantly reduced soluble TNF protein release into the supernatant and decreased total TNF protein levels in allergen-triggered RBL-2H3 cells[5]. Co-treatment of L929 cells with 1nM-10μM KP-457 and 20μM (-)-vinigrol for 16 hours reversed the antagonistic effect of (-)-vinigrol on

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TNF-α-induced cytotoxicity[6]. Treatment of mouse germinal vesicle stage oocytes with greater than 10μM KP-457 for 1.5 hours had no significant effect on oocyte-zona pellucida detachment scores[7].

References:

[1] Hirata S, Murata T, Suzuki D, et al. Selective Inhibition of ADAM17 Efficiently Mediates Glycoprotein Ibα Retention During Ex Vivo Generation of Human Induced Pluripotent Stem Cell-Derived Platelets. Stem Cells Transl Med. 2017 Mar;6(3):720-730.

[2] Tang R, Jin L, Chen C, et al. Mapping cell type-resolved transcriptomic profiles to patient survival in pancreatic cancer. Cancer Cell. 2026 Aug 10;44(8):1623-1638.e11.

[3] Lee DH, Yao C, Bhan A, et al. Integrative Genomic Analysis Reveals Four Protein Biomarkers for Platelet Traits. Circ Res. 2020 Oct 9;127(9):1182-1194.

[4] Six KR, Debaene C, Van den Hauwe M, et al. GPIbα shedding in platelets is controlled by strict intracellular containment of both enzyme and substrate. J Thromb Haemost. 2023 Aug;21(8):2223-2235.

[5] Ayo TE, Adhikari P, Xu H. TNFR1 links TNF exocytosis to TNF production in allergen-activated RBL-2H3 cells. Cell Signal. 2023 May;105:110607.

[6] Zhu Y, Wang L, Li J, et al. Photoaffinity labeling coupled with proteomics identify PDI-ADAM17 module is targeted by (-)-vinigrol to induce TNFR1 shedding and ameliorate rheumatoid arthritis in mice. Cell Chemical Biology. 2024 Mar 21;31(3):452-464.

[7] Macaulay AD, Ortman CS, Moore KR, et al. Initial detachment of the mouse oocyte from the zona pellucida is mediated by metallopeptidase activity. Biol Reprod. 2023 Jan 4;108(1):81-97.

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