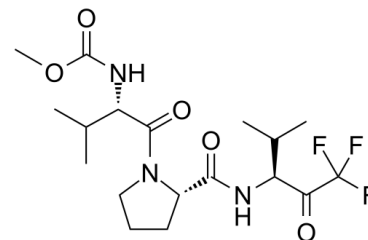


Data Sheet

Product Name:	ZD8321
Cat. No.:	CS-7453
CAS No.:	182073-77-4
Molecular Formula:	C ₁₈ H ₂₈ F ₃ N ₃ O ₅
Molecular Weight:	423.43
Target:	Elastase
Pathway:	Metabolic Enzyme/Protease
Solubility:	10 mM in DMSO



BIOLOGICAL ACTIVITY:

ZD8321 is a potent inhibitor of human **Neutrophil elastase (NE)** with a **K_i** of 13±1.7 nM. IC₅₀ & Target: K_i: 13±1.7 nM (Neutrophil elastase)^[1] **In Vitro:** TNFα-activated HUVEC is dose dependently inhibited by ZD8321. The adhesion between cancer cells with high elastase activity and TNFα-activated HUVEC is also inhibited by ZD8321. Expression of cell surface E-selectin by NE stimulation is suppressed in the presence of ZD8321. The concentration of soluble E-selectin in the medium increases after adhesive reaction between neutrophils and HUVEC. This increase is also dose dependently inhibited by ZD8321^[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: ^[2]HUVECs are cultured in RPMI 1640 containing 5% FBS for 6 h in collagen-coated, 24-well plates before the experiment. Some of the confluent HUVECs are further incubated with TNFα (1 ng/mL) and ZD8321 (0-50 mM), or with human NE (0-100ng/mL) for 4 h at 37°C. For adhesion assays, cancer cells resuspended in RPMI 1640 containing 5% FBS are added to each HUVEC-layered well. The plates are shaken at 700 rpm for 10 min at room temperature, washed twice with PBS, and examined by phase-contrast microscopy to determine the number of cells bound onto the HUVEC monolayer. The adhesive reactions of neutrophils to HUVEC are also analyzed in this manner^[2].

References:

- [1]. Veale CA, et al. Orally active trifluoromethyl ketone inhibitors of human leukocyte elastase. *J Med Chem.* 1997 Sep 26;40(20):3173-81.
[2]. Nozawa F, et al. Elastase activity enhances the adhesion of neutrophil and cancer cells to vascular endothelial cells. *J Surg Res.* 2000 Dec;94(2):153-8.

CAIndexNames:

L-Prolinamide, N-(methoxycarbonyl)-L-valyl-L-[(1S)-3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]-

SMILES:

COC(N[C@@H](C(C)C)C(N1[C@@H](CCC1)C(N[C@@H](C(C)C)C(C(F)(F)F)=O)=O)=O)=O

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

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