

Product Data Sheet

Product Name: TAPI-2
Cat. No.: GC19347

Chemical Properties

Cas. No. 187034-31-7

SMILES CC(C)(C)[C@@H](C(N[C@H](C(NCCN)=O)C)=O)NC(C(CC(NO)=O)CC(C)C)=O

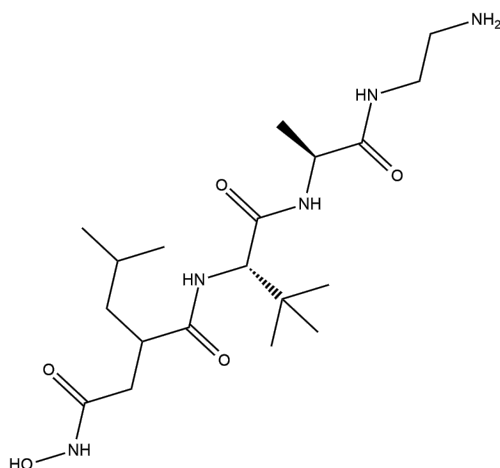
Formula $C_{19}H_{37}N_5O_5$ M.Wt 415.53

Solubility DMSO : ≥ 22 mg/mL (52.94 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

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

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Kinase experiment: Meprin activities are determined using N-benzoyl-L-tyrosyl p-aminobenzoic acid as substrate. The substrate concentration is 40 mM, and the enzyme concentration is always at least 10 times below K_i . Inhibitors are employed in a concentration range from 5 pM to 5 mM, depending on their inhibitory effect. Each inhibitor is tested over a concentration range covering at least ten different concentrations from $K_i/5$ to $5 \times K_i$. All reactions are carried out at 37°C in 50 mM Tris/HCl, pH 7.5, and 0.5 mM $MgCl_2$ [1].

Cell experiment: TAPI-2 is dissolved in DMSO and diluted with appropriate medium before use. All experiments are performed using 20 μ M TAPI-2. Cells are cultured with or without TAPI-2 for 48 hours and then seeded at 3,000 cells per well in 96-well plates. After pretreatment, increasing doses of 5-fluorouracil (5-FU) that are relevant to the recommended clinical dose (up to 2 μ g/mL) are added, with or without TAPI-2, for 72 hours. Cell viability is assessed by adding MTT substrate (0.25% in phosphate-buffered saline [PBS]) in growth medium (1:5 dilution) to cells for 1 hour at 37°C. The cells are washed with PBS, and 100 μ L of dimethyl sulfoxide is added. Optical density is measured at 570 nm, and relative MTT is presented as a percentage of control[2].

References:

- [1]. Kruse MN, et al. Human meprin alpha and beta homo-oligomers: cleavage of basement membrane proteins and sensitivity to metalloprotease inhibitors. *Biochem J.* 2004 Mar 1;378(Pt 2):383-9.
- [2]. Wang R, et al. A Disintegrin and Metalloproteinase Domain 17 Regulates Colorectal Cancer Stem Cells and Chemosensitivity Via Notch1 Signaling. *Stem Cells Transl Med.* 2016 Mar;5(3):331-8.

Background

TAPI-2 is a broad-spectrum inhibitor of matrix metalloprotease (MMP), tumour necrosis factor α -converting enzyme (TACE) and a disintegrin and metalloproteinase (ADAM), with an IC_{50} of 20 ± 10 μ M for MMP.

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The hydroxamate-based metalloprotease inhibitor TAPI-2 binds to hmeprin with inhibition constants IC_{50} 20 ± 10 μ M for hmeprin β subunit and 1.5 ± 0.27 nM for hmeprin α subunit. Generally, hmeprin α is inhibited more strongly than the β subunit[1]. Without affecting ADAM17 expression, TAPI-2 dramatically decreases the protein levels of NICD and its downstream target HES-1 in both HCP-1 and HT29 cells. Moreover, treating cells with TAPI-2 significantly decreases the CSC phenotype by - 50% in both CRC cell lines. The dose-dependent effects of TAPI-2 on the sphere formation and protein levels of NICD and HES-1 confirm that the concentration used (20 μ M) is within the effective dose range of TAPI-2 (5-40 μ M)[2].

References:

- [1]. Kruse MN, et al. Human meprin alpha and beta homo-oligomers: cleavage of basement membrane proteins and sensitivity to metalloprotease inhibitors. *Biochem J.* 2004 Mar 1;378(Pt 2):383-9.
- [2]. Wang R, et al. A Disintegrin and Metalloproteinase Domain 17 Regulates Colorectal Cancer Stem Cells and Chemosensitivity Via Notch1 Signaling. *Stem Cells Transl Med.* 2016 Mar;5(3):331-8.

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