# GI254023X

**Cat. No.:** HY-19956

**CAS No.:** 260264-93-5

**Molecular Formula:** $C_{21}H_{33}N_3O_4$

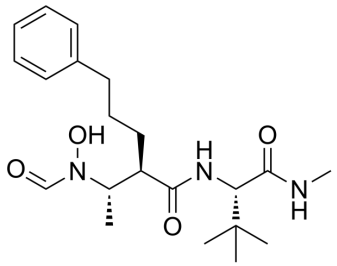
**Molecular Weight:** 391.5

**Target:** MMP

**Pathway:** Metabolic Enzyme/Protease

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 6 months |
| | -20°C | 1 month |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 100 mg/mL (255.43 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.5543 mL | 12.7714 mL | 25.5428 mL |
| | 5 mM | 0.5109 mL | 2.5543 mL | 5.1086 mL |
| | 10 mM | 0.2554 mL | 1.2771 mL | 2.5543 mL |

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

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.39 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.39 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.39 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

GI254023X is a potent MMP9 and ADAM10 inhibitor with $IC_{50}$s of 2.5 and 5.3 nM, respectively.

**$IC_{50}$ & Target**

IC50: 2.5 nM (MMP9), 5.3 nM (ADAM10)[1]

**In Vitro**

In cellular assay 25 μM and even a concentration of 1 μM GI254023X strongly reduces constitutive RAGE shedding; also PACAP-inducing shedding of RAGE is significantly reduced. At a concentration of 100 nM, a slight inhibition of RAGE shedding is still observed. In in vitro assays with recombinant proteinases, GI254023X discriminates between ADAM17 ($IC_{50}$=541 nM)

and ADAM10 ($IC_{50}$=5.3 nM)/MMP9 ($IC_{50}$=2.5 nM)[1]. CXCL16 shedding is inhibited by ADAM protease inhibitors (e.g GI254023x). A2780 cells are incubated with the ADAM-10/ADAM-17 inhibitor TAPI-2, as well as the ADAM-10-selective inhibitor GI254023x, as the level of expressed ADAM-10 is on average 9.8-fold higher on mRNA level compare with ADAM-17. In addition, GI254023x also prevents CXCL16 shedding from the cell membrane and is even more potent than TAPI-2[2]. When apply the specific ADAM10 (α-secretase) inhibitor GI254023X (5 mM) to serum/glucose-deprived slices, PI counts are significantly increased in comparison with DMSO (carrier)-treated controls[3].

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

## PROTOCOL

**Cell Assay** [3]

Cell death is quantified based on plasma membrane permeabilization. When apply the ADAM10 (a-secretase) inhibitor GI254023X (5 mM), slices are cultured in serum-/glucose-free medium for 48 h containing the inhibitor or its respective carrier (DMSO) as control. Round circles of identical size (Ø 500mm) are positioned in equivalent locations within the CA1 region of each hippocampus image and all PI-stained cells are counted using software. Cell viability assays are performed with a commercial kit according to the manufacturer's instructions. The assay quantitates ATP levels, an indicator of metabolically active cells, photometrically with a fluorescence plate reader. Additionally, the live-dead cell staining kit are applied according to the manual. Cells are simultaneously stained with green fluorescent calcein-AM (4mM; ex/em: 495/515 nm) to detect intracellular esterase activity (viable cells) and red fluorescent ethidium homodimer-3 (2mM; ex/em: 530/635 nm) to indicate loss of plasma membrane integrity (dead cells)[3].

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

## CUSTOMER VALIDATION

- Neuron. 2023 Apr 4;S0896-6273(23)00220-9.
- Elife. 2021 Sep 20;10:e67261.
- Genes Dis. 2020 Nov 21;8(6):867-881.
- Front Aging Neurosci. 2021 Apr 15;13:660249.
- Traffic. 2022 Nov 22.

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## REFERENCES


[1]. Verena V. Metz, et al. Induction of RAGE Shedding by Activation of G Protein-Coupled Receptors. PLoS One. 2012.

[2]. M J M Gooden, et al. Elevated serum CXCL16 is an independent predictor of poor survival in ovarian cancer and may reflect pro-metastatic ADAM protease activity. British Journal of Cancer (2014) 110, 1535–1544.

[3]. N Milosch, et al. Holo-APP and G-protein-mediated signaling are required for sAPPa-induced activation of the Akt. Cell Death Dis. 2014 Aug 28;5:e1391.





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