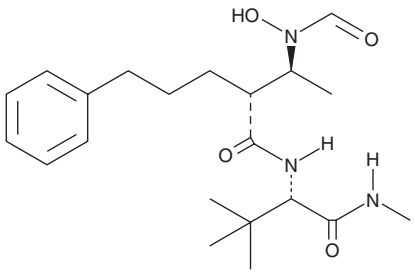
PRODUCT INFORMATION

GI 254023X

Item No. 28284

CAS Registry No.:	260264-93-5
Formal Name:	(αR)-N-[(1S)-2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-α-[(1S)-1-(formylhydroxyamino)ethyl]-benzenepentanamide
Synonyms:	GI 4023, SRI 028594
MF:	$C_{21}H_{33}N_3O_4$
FW:	391.5
Purity:	≥98%
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

GI 254023X is supplied as a crystalline solid. A stock solution may be made by dissolving the GI 254023X in the solvent of choice, which should be purged with an inert gas. GI 254023X is soluble in organic solvents such as ethanol and dimethyl formamide. The solubility of GI 254023X in these solvents is approximately 1 mg/ml.

GI 254023X is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, GI 254023X should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. GI 254023X has a solubility of approximately 0.14 mg/ml in a 1:6 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

GI 254023X is an inhibitor of the metalloproteinase-disintegrin ADAM10 (IC_{50} = 5.3 nM).[1] It is selective for ADAM10 over ADAM17, matrix metalloproteinase-1 (MMP-1), and MMP-3 (IC_{50}s = 541, 108, and 187 nM, respectively), but also inhibits MMP-9 and MMP-13 (IC_{50}s = 2.5 and 1.1 nM, respectively). GI 254023X inhibits constitutive shedding of CX3CL1, but not shedding induced by phorbol 12-myristate 13-acetate (PMA; Item No. 10008014), in COS-7 cells transfected with human chemokines (IC_{50}s = 0.4 and >10 µM, respectively). It also inhibits constitutive, but not PMA-induced, secretion of the IL-6 receptor (IL-6R) from THP-1 macrophages (IC_{50}s = 1.8 and >10 µM, respectively). GX 254023X (1 µM) decreases shedding of low density lipoprotein receptor-related protein 1 (LRP1) induced by amyloid-β (1-42) (Aβ42; Item No. 20574) in human brain microvessel endothelial cells (HBMECs) and increases Aβ42 transit across an *in vitro* blood brain barrier model in a concentration-dependent manner.[2] *In vivo*, GI 254023X (200 mg/kg) reduces brain LRP1 shedding and increases plasma levels of Aβ40 in a mouse model of Alzheimer's disease.

References

1. Ludwig, A., Hundhausen, C., Lambert, M.H., *et al.* Metalloproteinase inhibitors for the disintegrin-like metalloproteinases ADAM10 and ADAM17 that differentially block constitutive and phorbol ester-inducible shedding of cell surface molecules. *Comb. Chem. High Throughput Screen.* **8(2)**, 161-171 (2005).
2. Shackleton, B., Crawford, F., and Bachmeier, C. Inhibition of ADAM10 promotes the clearance of Aβ across the BBB by reducing LRP1 ectodomain shedding. *Fluids Barriers CNS* **13(1)**, 14 (2016).

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