

Product Data Sheet

Product Name: Cilengitide

Cat. No.: GC13559

Chemical Properties

Cas. No. 188968-51-6

Chemical Name 2-[(2S,5R,8S,11S)-5-benzyl-11-[3-(diaminomethylideneamino)propyl]-7-methyl-3,6,9,12,15-pentaoxo-8-propan-2-yl]-1,4,7,10,13-pentazacyclopentadec-2-yl]acetic acid

SMILES CC(C)C1C(=O)NC(C(=O)NCC(=O)NC(C(=O)NC(C(=O)N1C)CC2=CC=CC=C2)CC(=O)O)CCCN=C(N)N

Formula $C_{27}H_{40}N_8O_7$

M.Wt 588.66

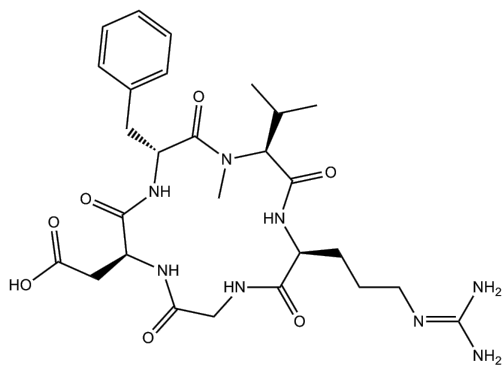
Solubility $\geq 29.433\text{mg/mL}$ in DMSO

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 A375 cells

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

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Preparation Method A375 cells were cultured in Dulbecco Modified Eagle Medium (DMEM) containing 10% fetal bovine serum (FBS) at 37°C and 5% CO₂ in a CO₂ incubator. The cells (6×10^3 per well) were seeded in a 96-well plate and cultured overnight. Subsequently, the cells were treated with Cilengitide at concentrations of 0, 1, 10, 100, and 1000 µg/ml. At 24 hours, 48 hours, and 72 hours after treatment, 10 µl of CCK-8 cell counting reagent was added to each well. After incubation at 37°C and 5% CO₂ for 2 hours, the absorbance value was measured at a wavelength of 450nm.

Reaction Conditions 0, 1, 10, 100, and 1000 µg/ml; 24, 48, and 72h

Applications Cilengitide treatment reduced cell viability of A375 cells in a dose- and time-dependent manner.

Animal experiment [2]:

Animal models Nude rats

Preparation Method Cells expressing light chain (LC) 3-green fluorescent protein (GFP) (4×10^5 cells/5 µl PBS) were injected at a rate of 0.5 µl/min into the right bregma of nude rats at a distance of 3mm. On the 21st day after tumor cell injection, Cilengitide (4mg/kg) was intraperitoneally injected, and the rats were sacrificed 48 hours later and the brain tissues were removed. The brain tissues were fixed with 10% formalin overnight and placed in a coronal brain tissue slide box, then cut into 2mm thick sections. The 2mm sections containing tumors were frozen in optimal cutting temperature (OCT) tissue blocks and subjected to autophagy-related immunofluorescence analysis.

Dosage form 4mg/kg for once; i.p.

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Applications Cilengitide significantly induced autophagy in the xenograft tumors of rat.

References:

- [1] Pan X, Yi M, Liu C, et al. Cilengitide, an $\alpha\beta3$ -integrin inhibitor, enhances the efficacy of anti-programmed cell death-1 therapy in a murine melanoma model[J]. Bioengineered, 2022, 13(2): 4557-4572.
- [2] Lomonaco S L, Finniss S, Xiang C, et al. Cilengitide induces autophagy-mediated cell death in glioma cells[J]. Neuro-oncology, 2011, 13(8): 857-865.

Background

Cilengitide, a cyclized pentapeptide, is a potent integrins antagonist with IC₅₀ values of 0.61nM, 8.4nM and 14.9nM for $\alpha\beta3$, $\alpha\beta5$, and $\alpha5\beta1$, respectively^[1]. Cilengitide inhibits binding of isolated $\alpha\beta3$ and $\alpha\beta5$ to vitronectin with an IC₅₀ value of 4 and 79nM, respectively^[2]. Cilengitide targets integrin dimers ITGAV:ITGB3 and ITGAV:ITGB5, and induces death in breast cancer cells with low integrin abundance^[3]. Cilengitide has been widely used in various cancer cell models to block integrin-mediated cell adhesion and migration^[4].

In vitro, Cilengitide treatment for 24 hours significantly inhibited the viability of A375 cells, with an IC₅₀ value of 5 μ g/ml^[5]. Treatment with 50 μ g/ml Cilengitide for 72 hours significantly inhibited the adhesion of HMEC-1 endothelial cells on the culture dish and induced cell apoptosis^[6]. Treatment with 100 μ g/ml Cilengitide for 3 days significantly inhibited the proliferation, migration and invasion of MDA-MB-231 cells^[7].

In vivo, Cilengitide treatment via daily intraperitoneal injection at a dose of 75mg/kg/day for 10 days, combined with two brain X-ray irradiations (5Gy; on the third and sixth days after tumor establishment), significantly inhibited the growth of brain tumors in mice and reduced tongue-like brain invasion^[8]. Forty-eight hours after a single intraperitoneal injection of 4mg/kg of Cilengitide into a rat model of glioma xenografts, significant autophagy was induced in the xenograft tumors^[9].

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- [1] Kapp T G, Rechenmacher F, Neubauer S, et al. A comprehensive evaluation of the activity and selectivity profile of ligands for RGD-binding integrins[J]. Scientific reports, 2017, 7(1): 39805.
- [2] Hariharan S, Gustafson D, Holden S, et al. Assessment of the biological and pharmacological effects of the $\alpha v \beta 3$ and $\alpha v \beta 5$ integrin receptor antagonist, cilengitide (EMD 121974), in patients with advanced solid tumors[J]. Annals of oncology, 2007, 18(8): 1400-1407.
- [3] Girnius N, Henstridge A Z, Marks B, et al. Cilengitide sensitivity is predicted by overall integrin expression in breast cancer[J]. Breast Cancer Research, 2024, 26(1): 187.
- [4] Reardon D A, Nabors L B, Stupp R, et al. Cilengitide: an integrin-targeting arginine–glycine–aspartic acid peptide with promising activity for glioblastoma multiforme[J]. Expert opinion on investigational drugs, 2008, 17(8): 1225-1235.
- [5] Pan X, Yi M, Liu C, et al. Cilengitide, an $\alpha v \beta 3$ -integrin inhibitor, enhances the efficacy of anti-programmed cell death-1 therapy in a murine melanoma model[J]. Bioengineered, 2022, 13(2): 4557-4572.
- [6] Oliveira-Ferrer L, Hauschild J, Fiedler W, et al. Cilengitide induces cellular detachment and apoptosis in endothelial and glioma cells mediated by inhibition of FAK/src/AKT pathway[J]. Journal of Experimental & Clinical Cancer Research, 2008, 27(1): 86.
- [7] Bretsch M, Merz M, Komljenovic D, et al. Cilengitide inhibits metastatic bone colonization in a nude rat model[J]. Oncology reports, 2011, 26(4): 843-851.
- [8] Wilisch-Neumann A, Kliese N, Pachow D, et al. The integrin inhibitor cilengitide affects meningioma cell motility and invasion[J]. Clinical Cancer Research, 2013, 19(19): 5402-5412.
- [9] Lomonaco S L, Finniss S, Xiang C, et al. Cilengitide induces autophagy-mediated cell death in glioma cells[J]. Neuro-oncology, 2011, 13(8): 857-865.

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