

## Product Data Sheet

Product Name: Cyclo (-RGDfK)

Cat. No.: GC17610

### Chemical Properties

Cas. No. 161552-03-0

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

SMILES C1C(=O)NC(C(=O)NC(C(=O)NC(C(=O)NC(C(=O)N1)CCCN=C(N)N)CCCCN)CC2=CC=CC=C2)CC(=O)O

Formula  $C_{27}H_{41}N_9O_7$

M.Wt 603.7

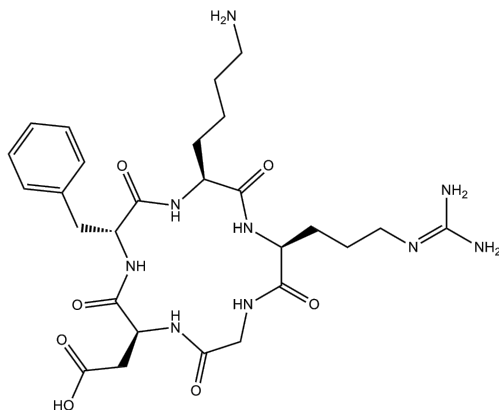
Solubility  $\geq 30.185\text{mg/mL}$  in DMSO,  $\geq 59.2\text{mg/mL}$  in Water

Storage Store at  $-20^\circ\text{C}$

General tips For obtaining a higher solubility, please warm the tube at  $37^\circ\text{C}$  and shake it in the ultrasonic bath for a while. Stock solution can be stored below  $-20^\circ\text{C}$  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 Rat thoracic artery smooth muscle cells (A7R5)

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A7R5 cells were seeded in 6-well plates at 80% confluence, serum-starved overnight, and then treated with Fibrinopeptide A (FPA,  $10^{-2}\mu\text{M}$ ) for 12h to establish the pro-atherogenic stimulation model. Cells were divided into three groups: control (serum-free DMEM), FPA group, and Cyclo(-RGDfK) (20nM) pre-treatment followed by FPA group.

Reaction Conditions 20nM; 1h pre-incubation at 37 °C followed by 12h FPA ( $10^{-2}\mu\text{M}$ ) exposure

Applications Cyclo(-RGDfK) significantly inhibited FPA-induced A7R5 migration and proliferation by blocking integrin  $\alpha\text{V}\beta 3$ , thereby down-regulating PI3K/AKT signaling and decreasing Cyclin D1 and PCNA expression.

### Animal experiment [2]:

Animal models Sprague-Dawley rats

SAH was induced by endovascular perforation. 1 h before modeling, rats received intranasal administration of 2.0 $\mu\text{g}$  cyclo(-RGDfK) dissolved in 4 $\mu\text{L}$  PBS; recombinant SPARC (0.3 $\mu\text{g}$ ) was given intracerebroventricularly 1h after SAH. Neurological scores, brain water content, IgG extravasation, and Western blot analyses were performed 24h post-SAH.

Dosage form 2.0 $\mu\text{g}$ ; IN

Applications Cyclo(-RGDfK) significantly ameliorated post-SAH blood–brain barrier disruption and neurological deficits by inhibiting integrin  $\alpha\text{V}\beta 3$ /MAPKs/MMP-9 signaling.

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### References:

- [1] Fang R, Yang Q, Wu D, et al. Fibrinopeptide a promotes the proliferation and migration of vascular smooth muscle cells by regulating the integrin  $\alpha$ V $\beta$ 3/PI3K/AKT signaling pathway. Mol Biol Rep. 2025 Feb 5;52(1):205.
- [2] Okada T, Suzuki H, Travis ZD, et al. SPARC Aggravates Blood-Brain Barrier Disruption via Integrin  $\alpha$ V $\beta$ 3/MAPKs/MMP-9 Signaling Pathway after Subarachnoid Hemorrhage. Oxid Med Cell Longev. 2021 Nov 11;2021:9739977.

### Background

Cyclo (-RGDfK) is a highly efficient and highly specific  $\alpha$ v $\beta$ 3 integrin inhibitor, with an IC<sub>50</sub> of only 0.94nM. Cyclo(-RGDfK) can precisely target the  $\alpha$ v $\beta$ 3 integrin on the surface of tumor cells<sup>[1]</sup>. Thereby Cyclo(-RGDfK) is therefore widely used in studies targeting tumor neovasculature and cancer cells<sup>[2]</sup>. Cyclo(-RGDfK) can inhibit cancer cell proliferation and migration<sup>[3]</sup>. Moreover, Cyclo(-RGDfK) is frequently employed as a core ligand for constructing  $\alpha$ v $\beta$ 3-targeted imaging probes or drug delivery systems in tumor imaging studies<sup>[4]</sup>.

In vitro, pretreatment of HepG2 and A549 cells with Cyclo(-RGDfK) (1–10 $\mu$ M) for 4–6h significantly enhanced cellular uptake of the cRGD-PEG-g-(PBYP-ss-CPT) nanoprodrug; compared to the non-cRGD control group, intracellular drug accumulation increased and cell viability was significantly reduced<sup>[5]</sup>. Pretreatment of A7R5 cells with Cyclo(-RGDfK) (20nM) for 1h followed by 12h stimulation with FPA (10<sup>-2</sup> $\mu$ M) significantly inhibited cell migration and proliferation, downregulated integrin  $\alpha$ v $\beta$ 3/PI3K/AKT pathway-related protein expression, and reduced Cyclin D1 and PCNA levels<sup>[6]</sup>.

In vivo, intranasal administration of Cyclo(-RGDfK) (2.0 $\mu$ g) 1h prior to modeling significantly inhibited integrin  $\alpha$ v $\beta$ 3/MAPKs/MMP-9 pathway activation, alleviated blood–brain barrier disruption, and improved neurological deficits in a rat model of subarachnoid hemorrhage (SAH)<sup>[7]</sup>. Cyclo(-RGDfK)-conjugated gold nanoshells (400mg/kg) were injected intravenously into HCT116 colon cancer-bearing nude mice; 24h later, near-infrared laser thermotherapy (47°C  $\times$  10min) significantly enhanced tumor vascular-targeted thermal ablation, resulting in more extensive necrosis and vascular disruption<sup>[8]</sup>.

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- [1] Simeček J, Notni J, Kapp TG, et al. Benefits of NOPO as chelator in gallium-68 peptides, exemplified by preclinical characterization of (68)Ga-NOPO-c(RGDfK). *Mol Pharm*. 2014 May 5;11(5):1687-95.
- [2] Jin ZH, Furukawa T, Degardin M, et al.  $\alpha V\beta 3$  Integrin-Targeted Radionuclide Therapy with  $^{64}\text{Cu}$ -cyclam-RAFT-c(-RGDfK)-4. *Mol Cancer Ther*. 2016 Sep;15(9):2076-85.
- [3] Kalaydina RV, Zhou H, Markvicheva E, et al. Impact of Fucosylation on Self-Assembly of Prostate and Breast Tumor Spheroids by Using Cyclo-RGDfK(TPP) Peptide and Image Object Detection. *Onco Targets Ther*. 2019 Dec 17;12:11153-11173.
- [4] Yoshimoto M, Hayakawa T, Mutoh M, et al. In vivo SPECT imaging with  $^{111}\text{In}$ -DOTA-c(RGDfK) to detect early pancreatic cancer in a hamster pancreatic carcinogenesis model. *J Nucl Med*. 2012 May;53(5):765-71.
- [5] Zhou R, Zhang M, He J, et al. Functional cRGD-Conjugated Polymer Prodrug for Targeted Drug Delivery to Liver Cancer Cells. *ACS Omega*. 2022 Jun 7;7(24):21325-21336.
- [6] Fang R, Yang Q, Wu D, et al. Fibrinopeptide promotes the proliferation and migration of vascular smooth muscle cells by regulating the integrin  $\alpha V\beta 3$ /PI3K/AKT signaling pathway. *Mol Biol Rep*. 2025 Feb 5;52(1):205.
- [7] Okada T, Suzuki H, Travis ZD, et al. SPARC Aggravates Blood-Brain Barrier Disruption via Integrin  $\alpha V\beta 3$ /MAPKs/MMP-9 Signaling Pathway after Subarachnoid Hemorrhage. *Oxid Med Cell Longev*. 2021 Nov 11;2021:9739977.
- [8] Xie H, Diagaradjane P, Deorukhkar AA, et al. Integrin  $\alpha v\beta 3$ -targeted gold nanoshells augment tumor vasculature-specific imaging and therapy. *Int J Nanomedicine*. 2011;6:259-69.

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