

Product Data Sheet

Product Name: A 779
Cat. No.: GC11004

Chemical Properties

Cas. No. 159432-28-7

Chemical Name (2R,3Z,5S,6Z,8S,9Z,11S,12Z,14S,15Z,17S,18Z,20S)-5-((1H-imidazol-5-yl)methyl)-20-amino-8-((S)-sec-butyl)-17-(3-guanidinopropyl)-4,7,10,13,16,19-hexahydroxy-11-(4-hydroxybenzyl)-14-isopropyl-2-methyl-3,6,9,12,15,18-hexaazadocosa-3,6,9,12,15,18-hexaene-1,22-

SMILES CC[C@]([C@@]([N=C(O)/[C@]([N=C(O)/[C@]([N=C(O)/[C@]([N=C(O)/[C@](N)([H])CC(O)=O)([H])CCCNC(N)=N)([H])C(C)C)([H])CC1=CC=C(O)C=C1)([H])/C(O)=N/[C@@]([C(O)=N/[C@](C(O)=O)([H])C)([H])CC2=CN=CN2)([H])C

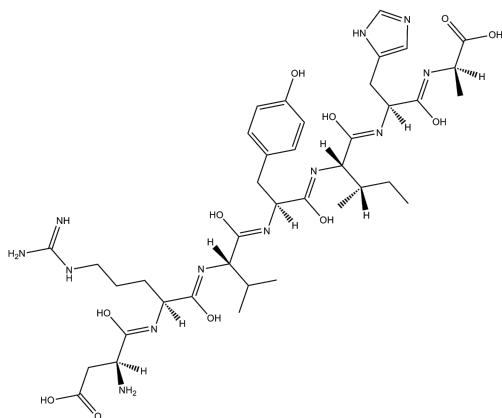
Formula C₃₉H₆₀N₁₂O₁₁ M.Wt 872.97

Solubility ≥ 29.1mg/mL in Water with gentle warming 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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Cell experiment [1]:

Cell lines MIN6 cells

Preparation Method Mouse pancreatic β -cell line MIN6 cells were digested with 0.25% trypsin into individual cells and passaged at a ratio of 1:3. Following groups were made: (1) Normal control group (Con, 11.1mM glucose), (2) high glucose group (HG group, 33.3mM glucose), (3) HG+ Ang-(1-7) group [33.3mM glucose + 1nM Ang-(1-7)], (4) HG+ Ang-(1-7)+ A 779 group (33.3mM glucose + 1nM Ang-(1-7) + 1nM A 779), and (5) HG+ Ang-(1-7) + LY294002 group (33.3mM glucose + 1nM Ang-(1-7) + 50uM LY294002). Four replicate wells were used in each group. After 48h of cell culture in each group, the expression levels of cell-specific markers Pdx1, MafA, Oct4 and Nanog in each group were detected by Real-time PCR and Western blot. The expression levels of pathway-related proteins Akt, p-Akt, FoxO1, and p-FoxO1 protein levels in each group were detected by Western blot.

Reaction
Conditions 1nM ; 48h

Applications A 779 reverse Ang-(1-7) 's effect on preventing high glucose-induced pathological dedifferentiation of pancreatic β -cell.

Animal experiment [2]:

Animal models C57BL/6 male mice

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Ventilator-induced lung injury (VILI) was induced in mice by mechanical ventilation (MV) by regulating the tidal volume. Endoplasmic reticulum stress (ERS) was inhibited by tracheal instillation of 4-phenylbutyric acid (4-PBA) (1 mg/kg). ACE2's enzymatic function was activated or inhibited by subcutaneous Preparation Method injection of resorcinolnaphthalein (RES, 20µg/kg) or MLN-4760 (20µg/kg). pGLV-EF1a-GFP-ACE2 was instilled into the trachea to increase the protein expression of ACE2. The Ang (1-7) receptor, Mas, was antagonized by injecting A 779 subcutaneously (80µg/kg) 6h before MV. Then ACE2 protein levels, Ang-(1-7) levels and ERS were detected.

Dosage form 80µg/kg; s.c.

Applications A 779 blocked the inhibitory effects of angiotensin converting enzyme 2 (ACE2) on endoplasmic reticulum stress (ERS) in Ventilator-induced lung injury.

References:

- [1] Guo H, Guo D, An M, Zhang R, Wang C, He J. Angiotensin-(1-7) Improves Islet β -cell Dedifferentiation by Activating PI3K/Akt/FoxO1 Pathway. *Protein Pept Lett.* 2023;30(12):1009-1019.
- [2] Lin X, Zhuang Y, Gao F. ACE2 Alleviates Endoplasmic Reticulum Stress and Protects against Pyroptosis by Regulating Ang1-7/Mas in Ventilator-Induced Lung Injury. *Front Biosci (Landmark Ed).* 2024;29(9):334.

Background

A 779 is a potent and selective angiotensin-(1-7)/Mas receptor antagonist with an IC₅₀ value of 0.3nM^[1]. Angiotensin-(1-7) (Ang-(1-7)) is an endogenous ligand for the G protein-coupled receptor, a bioactive peptide within the renin-angiotensin system (RAS) that significantly contributes to maintaining cardiovascular homeostasis and hydroelectrolyte balance in physiological and pathologic conditions^{[1][2]}. A 779 inhibit the biological effects of Ang-(1-7) by binding to the G protein-coupled receptor Mas receptor (MasR)^[3].

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In vitro, pretreatment of human umbilical vein endothelial cells (HUVECs) with 1 μ M A 779 for 30 minutes significantly inhibited Ang-(1-7)'s effect on attenuating ox-LDL induced injury by modulating the specific Mas receptors^[4]. Treatment of mouse islet β -cell line MIN6 cells with 1 nM A 779 for 48h reverse Ang-(1-7)'s effect on preventing high glucose-induced pathological dedifferentiation of pancreatic β -cell^[5].

In vivo, A 779 considerably eradicate the defensive properties of Ang-(1-7) on bone metabolism, mineralization and micro-structure after it was delivered at infusion rate of 400ng kg⁻¹ min⁻¹ for 6 weeks in an ovariectomized (OVX) rodent model of osteoporosis^{[6][7]}. Subcutaneous injection of A 779(80 μ g/kg) block the inhibitory effects of angiotensin converting enzyme 2 (ACE2) on endoplasmic reticulum stress (ERS) and pyroptosis in Ventilator-induced lung injury^[8].

References:

- [1] Santos RA, Simoes e Silva AC, Maric C, et al. Angiotensin-(1-7) is an endogenous ligand for the G protein-coupled receptor Mas. Proc Natl Acad Sci U S A. 2003;100(14):8258-8263.
- [2] Maia LG, Ramos MC, Fernandes L, de Carvalho MH, Campagnole-Santos MJ, Souza dos Santos RA. Angiotensin-(1-7) antagonist A-779 attenuates the potentiation of bradykinin by captopril in rats. J Cardiovasc Pharmacol. 2004;43(5):685-691.
- [3] Santos RA, Campagnole-Santos MJ, Baracho NC, et al. Characterization of a new angiotensin antagonist selective for angiotensin-(1-7): evidence that the actions of angiotensin-(1-7) are mediated by specific angiotensin receptors. Brain Res Bull. 1994;35(4):293-298.
- [4] Yan WF, Xue JJ, Yang HY, Liang B, Yang ZM. Effects and related mechanism of angiotensin-(1-7) on Toll-like receptor 4-mediated oxidative stress in human umbilical vein endothelial cells. Zhonghua Xin Xue Guan Bing Za Zhi. 2017;45(3):223-229.
- [5] Guo H, Guo D, An M, Zhang R, Wang C, He J. Angiotensin-(1-7) Improves Islet β -cell Dedifferentiation by Activating PI3K/Akt/FoxO1 Pathway. Protein Pept Lett. 2023;30(12):1009-1019.
- [6] Abuhashish HM, Ahmed MM, Sabry D, Khat tab MM, Al-Rejaie SS. Angiotensin (1-7) ameliorates the structural and biochemical alterations of ovariectomy-induced osteoporosis in rats via activation of ACE-2/Mas receptor axis. Sci Rep. 2017;7(1):2293.
- [7] Abuhashish HM, Ahmed MM, Sabry D, Khat tab MM, Al-Rejaie SS. ACE-2/Ang1-7/Mas cascade mediates ACE inhibitor, captopril, protective effects in estrogen-deficient osteoporotic rats. Biomed Pharmacother. 2017;92:58-68.
- [8] Lin X, Zhuang Y, Gao F. ACE2 Alleviates Endoplasmic Reticulum Stress and Protects against

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Pyroptosis by Regulating Ang1-7/Mas in Ventilator-Induced Lung Injury. Front Biosci (Landmark Ed). 2024;29(9):334.

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