

Product Data Sheet

Product Name: Aprotinin
 Cat. No.: GC12900

Chemical Properties

Cas. No. 9087-70-1

SMILES CC(O)=O.CC.CC.CCcC.[R].[P].[2H].[L].[E].[P].[P].[Y].[3H].[G].[KH].[R].[R].[Y].F.[Y].[*].[L].F.[V].[Y].[G].[G].[R].[KH].[R].N.N.F.[KH].S.[*].[2H].[R].[G].[G].[*].[KH].[*].[3H].C.[*].F.[P].[*].I.I.N.[Q].[3H].[M]

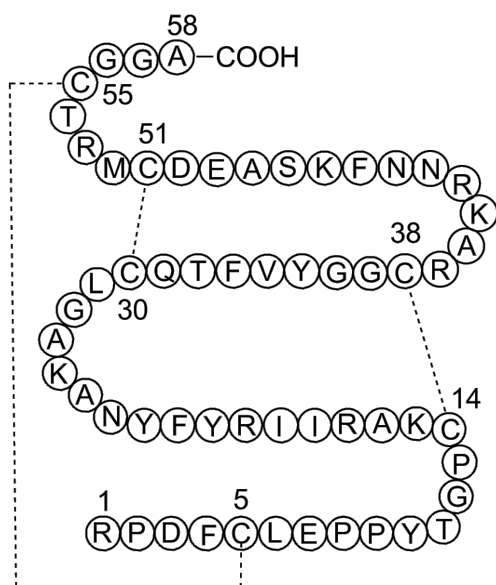
Formula $C_{284}H_{432}N_{84}O_{79}S_7$ M.Wt 6511.44

Solubility $\geq 195\text{mg/mL}$ in Water Storage Store at 2-8°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]:

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Cell lines	Human umbilical vein endothelial cells (HUVECs)
Preparation Method	HUVECs were cultured in M199 medium supplemented with 15% fetal bovine serum and 150µg/ml endothelial cell growth supplement, 5U/ml heparin sodium, 100U/ml penicillin, 100µg/ml streptomycin, and 50µg/ml gentamycin in a humidified incubator containing 5% CO ₂ at 37°C. Cells were seeded in a 6-well plate at a density of 1×10 ⁴ cells/well overnight. Cells were treated with different concentrations of Aprotinin (0, 20, 50, 100, and 200U/ml) for 24h. Cells and cell-conditioned culture medium were used for Western blot analysis.
Reaction Conditions	0, 20, 50, 100, and 200U/ml; 24h
Applications	Aprotinin treatment enhanced the Pleiotrophin levels in HUVECs in a dose-dependent manner.

Animal experiment [2]:

Animal models	129S1/SvImJ mice
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Preparation Method	129S1/SvImJ mice (6-month-old) were maintained in a controlled environment at 22-24°C and 60% relative humidity under a 12h light/dark cycle, and were given free access to food and water. Before the experiment began, all the mice were individually housed in metabolic cages (with a diameter of 20cm and an area of 314cm²) and were fed with control feed (containing 106μmol/g of sodium) for 2 days. Thereafter, mice underwent implantation of custom-made pellets with a matrix-driven sustained release of Aprotinin or placebo. These pellets were surgically implanted subcutaneously on the back of the mice under isoflurane anesthesia. After the operation, the wound conditions and the suture were checked several times. Subsequently, mice were studied in a 2×2 factorial design over 10 days in the metabolic cage. Mice in groups 1 and 2 continued to receive the control diet with an aprotinin-containing or placebo pellet, respectively. Mice in groups 3 and 4 were switched to a low-salt diet (sodium content: 7μmol/g) with or without Aprotinin-containing or a placebo pellet, respectively. The assignment to the respective group was random. The total Aprotinin dose of the pellets was 2mg (6000kIU/mg) per day to be delivered over a maximum of 10 days. The kidney tissues of the mice were collected for analysis.
Dosage form	2mg/day; 10 days; s.c.
Applications	Aprotinin treatment caused damage to the renal proximal tubular in mice on a low-sodium diet and impaired renal function.

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- [1] Koutsoumpa M, Hatzia Apostolou M, Mikelis C, et al. Aprotinin stimulates angiogenesis and human endothelial cell migration through the growth factor pleiotrophin and its receptor protein tyrosine phosphatase β/ζ [J]. European journal of pharmacology, 2009, 602(2-3): 245-249.
- [2] Woerner S, Bohnert B N, Woern M, et al. Renal effects of the serine protease inhibitor aprotinin in healthy conscious mice[J]. Acta Pharmacologica Sinica, 2022, 43(1): 111-120.

Background

Aprotinin is a naturally occurring serine protease inhibitor that inhibits plasmin and kallikrein with K_i values of 0.07nM and 36nM, respectively^[1]. Aprotinin competitively suppresses nitric oxide synthase (NOS)-I and NOS-II with K_i values of 50 μ M and 78 μ M, respectively, at pH 7.5 and 37.0°C^[2]. Aprotinin hinders fibrinolytic pathways to reduce the formation of fibrin degradation products, and improves haemostasis during and after cardiopulmonary bypass by preserving the platelet membrane adhesive receptor^[3]. Aprotinin has been widely used in antiviral research to impede the serine proteases responsible for activating the influenza virus, thereby blocking the replication of the avian influenza virus^[4].

In vitro, Aprotinin treatment (100U/ml) for 24 hours stimulated cell migration and increased the content of full-length Pleiotrophin in LNCaP cells^[5]. Pretreatment with Aprotinin at 1600kIU/ml for 1 hour inhibited 2ng/ml TNF- α -induced ICAM-1 and VCAM-1 expression in human umbilical vein endothelial cells (HUVECs)^[6]. Treatment with 100kIU/ml Aprotinin for 24 hours decreased the mouse neuronal cell death induced by N-methyl-D-aspartate^[7].

In vivo, Aprotinin administration via subcutaneous injection at a dose of 2mg/day for 10 days impaired the proximal renal tubular function of 129S1/SvImJ mice with a low-salt diet, resulting in increased glycosuria and proteinuria excretion^[8]. A single intravenous injection of Aprotinin at a dose of 60000kIU/kg via the tail vein 15 minutes before the onset of ischemia reduced ischemia-reperfusion-induced elevations in serum creatinine and alleviated renal inflammation in rats^[9].

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- [2] Venturini G, Colasanti M, Ascenzi P. Aprotinin, the first competitive protein inhibitor of NOS activity[J]. Biochemical and Biophysical Research Communications, 1998, 249(1): 263-265.
- [3] Davis R, Whittington R. Aprotinin: a review of its pharmacology and therapeutic efficacy in reducing blood loss associated with cardiac surgery[J]. Drugs, 1995, 49(6): 954-983.
- [4] Zhirnov O P, Klenk H D, Wright P F. Aprotinin and similar protease inhibitors as drugs against influenza[J]. Antiviral research, 2011, 92(1): 27-36.
- [5] Koutsioumpa M, Hatzia Apostolou M, Mikelis C, et al. Aprotinin stimulates angiogenesis and human endothelial cell migration through the growth factor pleiotrophin and its receptor protein tyrosine phosphatase β/ζ [J]. European journal of pharmacology, 2009, 602(2-3): 245-249.
- [6] Asimakopoulos G, Lidington E A, Mason J, et al. Effect of aprotinin on endothelial cell activation[J]. The Journal of thoracic and cardiovascular surgery, 2001, 122(1): 123-128.
- [7] Iwata Y, Nicole O, Okamura T, et al. Aprotinin confers neuroprotection by reducing excitotoxic cell death[J]. The Journal of Thoracic and Cardiovascular Surgery, 2008, 135(3): 573-578.
- [8] Woerner S, Bohnert B N, Woern M, et al. Renal effects of the serine protease inhibitor aprotinin in healthy conscious mice[J]. Acta Pharmacologica Sinica, 2022, 43(1): 111-120.
- [9] Kher A, Meldrum K K, Hile K L, et al. Aprotinin improves kidney function and decreases tubular cell apoptosis and proapoptotic signaling after renal ischemia-reperfusion[J]. The Journal of Thoracic and Cardiovascular Surgery, 2005, 130(3): 662. e1-662. e11.

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