# Product Data Sheet

Product Name: Angiotensin 1/2 (1-9)
Cat. No.: GP10025

## Chemical Properties

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| Cas. No. | 34273-12-6 |
| Chemical Name | Angiotensin 1/2 (1-9) |
| SMILES | CCC(C)C(C(=O)NC(CC1=CN=CN1)C(=O)N2CCCC2C(=O)NC(CC3=CC=CC=C3)C(=O)NC(CC4=CN=CN4)C(=O)O)NC(=O)C(CC5=CC=C(C=C5)O)NC(=O)C(C(C)C)NC(=O)C(CCCN=C(N)N)NC(=O)C(CC(=O)O)N |

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| Formula | $C_{56}H_{78}N_{16}O_{13}$ | M.Wt | 1183.32 |
| Solubility | ≥118.3mg/mL in DMSO | Storage | Store at -20°C |

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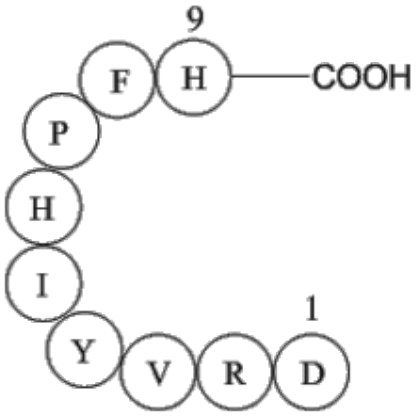
| General tips | For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months. |
| Shipping Condition | Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request. |

Structure




## Protocol

| **Cell experiment [1]:** |
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| Cell lines | Human umbilical vascular endothelial cells (HUVECs) |
| Preparation Method | HUVECs were cultured in DMEM medium, supplemented with 10% fetal bovine serum, 100U/ml penicillin, and 100μg/ml streptomycin at 37°C in an incubator with 5% $CO_2$. Cells were inoculated in a 96-well plate at a density of $3\times10^4$ cells/ml. After serum starvation, cells were pretreated with different concentrations of Angiotensin 1/2 (1-9) (0, 25, 50, 75, and 100μM) for 1h and followed by Ang II (10μM) for 24h, and cell viability was assessed. |
| Reaction Conditions | 0, 25, 50, 75, and 100μM; 1h |
| Applications | Angiotensin 1/2 (1-9) treatment markedly mitigated Ang II-induced cell death in HUVECs in a dose-dependent manner. |
| **Animal experiment [2]:** | |
| Animal models | Male Sprague-Dawley (SD) rats |

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| Preparation Method | Male Sprague-Dawley (SD) rats (2 months old) were housed at controlled temperature (23-25°C), humidity (50%), and lighting (12h light/dark cycle) with food and water provided ad libitum. Rats were randomized to receive either 55mg/kg of STZ diluted in 0.1M citrate buffer, pH 4.5 (diabetic) to induce experimental type 1 diabetes or citrate buffer alone (non-diabetic control) by tail vein injection following overnight fasting. The diabetic state was confirmed 72h later by the determination of blood glucose concentrations ≥16.7mM. Four weeks later, osmotic minipumps were subcutaneously implanted to deliver Angiotensin 1/2 (1-9) (200ng/kg/min), or Mas antagonist A779 (100ng/kg/min) for 4 weeks. At the end of the treatment period, the animals were kept on an overnight fast and were euthanized via an anaesthetic overdose. Hearts were excised for analysis. |
| Dosage form | 200ng/kg/min; 4 weeks; s.c. |
| Applications | Angiotensin 1/2 (1-9) treatment attenuated cardiac hypertrophy, reduced cardiac fibrosis, and improved ventricular function in diabetic rats. |
| References:[1] Guo C, Liu H, Li B, et al. Angiotensin-(1–9) prevents angiotensin II-induced endothelial apoptosis through CNPY2/PERK pathway[J]. Apoptosis, 2023, 28(3): 379-396.[2] Zheng H, Pu S Y, Fan X F, et al. Treatment with angiotensin-(1-9) alleviates the cardiomyopathy in streptozotocin-induced diabetic rats[J]. Biochemical pharmacology, 2015, 95(1): 38-45. | |

## Background

Angiotensin 1/2 (1-9) is a competitive inhibitor of Angiotensin-Converting Enzyme 2 (ACE2) that regulates cardiovascular remodeling[1]. Angiotensin 1/2 (1-9) inhibits cardiomyocyte hypertrophy via the Mas and Angiotensin type 2 receptor, and stimulates atrial natriuretic peptide (ANP) secretion via the AT2R-PI3K-Akt-NO-cGMP pathway[2]. Angiotensin 1/2 (1-9) has been widely used for the prevention and improvement of cardiovascular damage caused by activation of the renin-angiotensin system[3].

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In vitro, Angiotensin 1/2 (1-9) treatment (1nM) for 48 hours resulted in a decrease in the number of cells in the G0/G1 phase and an increase in the number of cells in the S phase, and promoted cell migration in PNT1A cells[4]. Pretreatment with 1μM Angiotensin 1/2 (1-9) for 30 minutes inhibited fibroblast proliferation stimulated by serum[5]. 100μM of Angiotensin 1/2 (1-9) pre-incubation for 1 hour suppressed the apoptosis of human umbilical vein endothelial cells (HUVECs) induced by Ang II, increased cell viability and reduced the protein levels of Bax and cleaved-caspase-3[6].

In vivo, continuous administration of Angiotensin 1/2 (1-9) at a dose of 200ng/kg/min via a subcutaneously implanted osmotic minipump for 4 weeks alleviated myocardial hypertrophy, reduced myocardial fibrosis, and improved ventricular function in streptozotocin-induced diabetic rats[7]. Continuous administration of Angiotensin 1/2 (1-9) at a dose of 1200ng/kg/min via a subcutaneously implanted osmotic minipump for 14 days reduced blood pressure and alleviated vascular remodeling in spontaneously hypertensive rats[8].

References:
[1] Ocaranza M P, Jalil J E. Protective role of the ACE2/Ang-(1–9) axis in cardiovascular remodeling[J]. International journal of hypertension, 2012, 2012(1): 594361.
[2] Cha S A, Park B M, Gao S, et al. Stimulation of ANP by angiotensin-(1-9) via the angiotensin type 2 receptor[J]. Life sciences, 2013, 93(24): 934-940.
[3] Ocaranza M P, Michea L, Chiong M, et al. Recent insights and therapeutic perspectives of angiotensin-(1–9) in the cardiovascular system[J]. Clinical science, 2014, 127(9): 549-557.
[4] Domińska K, Kowalska K, Habrowska-Górczyńska D E, et al. The opposite effects of angiotensin 1-9 and angiotensin 3-7 in prostate epithelial cells[J]. Biochemical and biophysical research communications, 2019, 519(4): 868-873.
[5] Flores-Munoz M, Work L M, Douglas K, et al. Angiotensin-(1-9) attenuates cardiac fibrosis in the stroke-prone spontaneously hypertensive rat via the angiotensin type 2 receptor[J]. Hypertension, 2012, 59(2): 300-307.
[6] Guo C, Liu H, Li B, et al. Angiotensin-(1–9) prevents angiotensin II-induced endothelial apoptosis through CNPY2/PERK pathway[J]. Apoptosis, 2023, 28(3): 379-396.
[7] Zheng H, Pu S Y, Fan X F, et al. Treatment with angiotensin-(1-9) alleviates the cardiomyopathy in streptozotocin-induced diabetic rats[J]. Biochemical pharmacology, 2015, 95(1): 38-45.
[8] Norambuena-Soto I, Ocaranza M P, Cancino-Arenas N, et al. Angiotensin-(1–9) prevents vascular remodeling by decreasing vascular smooth muscle cell dedifferentiation through a FoxO1-dependent

mechanism[J]. Biochemical pharmacology, 2020, 180: 114190.