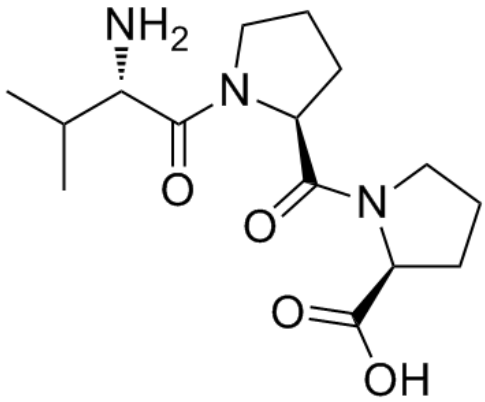
Product Data Sheet

Product Name: H-Val-Pro-Pro-OH
Cat. No.: GC31529

Chemical Properties

Cas. No.	58872-39-2		
Formula	$C_{15}H_{25}N_3O_4$	M.Wt	311.38
Solubility	125 mg/mL in Water(Need ultrasonic)	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 HepG2 cells

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Preparation Method	HepG2 cells were cultured in a minimal essential medium (MEM) supplemented with 10% fetal bovine serum, 100μg/ml streptomycin, 100U/ml penicillin and 1% pyruvate sodium, under a humidified environment of 37°C and 5% CO_2. HepG2 cells were seeded at a density of 1×10^5 cells per well in a 96-well plate. After incubation for 24 hours, the culture medium was discarded. Then, the cells were treated with H-Val-Pro-Pro-OH (600μM) in the presence of 10mM glucose for 18 hours, and the glucose metabolism enzymes and glucose consumption were measured.
Reaction Conditions	600μM; 18h
Applications	H-Val-Pro-Pro-OH significantly increased the glucose consumption of HepG2 cells and reduced the activity of Phosphoenolpyruvate carboxykinase.

Animal experiment [2]:

Animal models	Male Wistar rat
Preparation Method	7-week-old male Wistar rats were acclimated for 1 week in a room with controlled temperature (23°C), humidity (55%), and lighting (12:12 hours light-dark cycle), and rats were allowed to freely access food and tap water. Based on the body weight, the rats were randomly divided into 3 groups. The first group (control group) drank untreated drinking water. The second group (L-NAME group) drank L-NAME dissolved in the drinking water (1g/l, 100mg/kg/day). The third group (L-NAME + VPP group) drank L-NAME (1g/l) and H-Val-Pro-Pro-OH (0.3g/l, 30mg/kg/day), for a duration of 8 weeks. The hearts and kidneys of the rats were collected for histopathological analysis.
Dosage form	30mg/kg/day for 8 weeks; p.o.

Caution: Product has not been fully validated for medical applications. For research use only.
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Applications	H-Val-Pro-Pro-OH treatment alleviated the left ventricular hypertrophy, abnormal glomerular morphology and thickening of small arteries in the kidneys caused by L-NAME in rats.

References:
[1] Wang C, Zheng L, Zhao M. Molecular targets and mechanisms of casein-derived tripeptides Ile-Pro-Pro and Val-Pro-Pro on hepatic glucose metabolism[J]. Journal of Agricultural and Food Chemistry, 2023, 71(48): 18802-18814.
[2] Nonaka A, Nakamura T, Hirota T, et al. The milk-derived peptides Val-Pro-Pro and Ile-Pro-Pro attenuate arterial dysfunction in L-NAME-treated rats[J]. Hypertension Research, 2014, 37(8): 703-707.

Background

H-Val-Pro-Pro-OH is a milk-derived tripeptide that inhibits Angiotensin I converting enzyme (ACE), with an IC_{50} of 9μM[1]. H-Val-Pro-Pro-OH can stimulate insulin signaling, especially phosphorylation of protein kinase B and insulin receptor (IR), to ameliorate insulin resistant[2]. H-Val-Pro-Pro-OH has been widely used in different animal models to regulate immune function and inhibit inflammatory responses[3].

In vitro, H-Val-Pro-Pro-OH pretreatment (50μM) for 12 hours can significantly inhibit the proliferation of vascular smooth muscle cells (VSMCs) induced by angiotensin II (Ang II)[4]. Treatment with 600μM H-Val-Pro-Pro-OH for 18 hours significantly enhanced glucose consumption in HepG2 cells, regulated the activity of glucose metabolism enzymes, and increased the protein levels of phosphorylated AKT (p-AKT) and GLUT2 in HepG2 cells[5]. Treatment with H-Val-Pro-Pro-OH (50μM) for 72 hours significantly increased lipid accumulation in 3T3-F442A cells, leading to a significant increase in PPARγ and adiponectin expression[6].

In vivo, H-Val-Pro-Pro-OH treatment via oral administration at a dose of 30mg/kg/day for 8 weeks alleviated the left ventricular hypertrophy, abnormal glomerular morphology and thickening of small arteries in the kidneys caused by N(G)-nitro-L-arginine methyl ester hydrochloride (L-NAME) in rats[7]. Oral administration of 125.4μmol/kg/day of H-Val-Pro-Pro-OH daily for 31 consecutive weeks

delayed the development of atherosclerosis in male apoE(-/-) mice and reduced the expression of inflammatory factors[8].

References:
[1] Nakamura Y, Yamamoto N, Sakai K, et al. Purification and characterization of angiotensin I-converting enzyme inhibitors from sour milk[J]. Journal of dairy science, 1995, 78(4): 777-783.
[2] Li S, Bu T, Zheng J, et al. Preparation, bioavailability, and mechanism of emerging activities of Ile-Pro-Pro and Val-Pro-Pro[J]. Comprehensive Reviews in Food Science and Food Safety, 2019, 18(4): 1097-1110.
[3] Pérez-Vielma N M, Gómez-López M, Maldonado J, et al. Recognition of the interaction between the bioactive peptide Val–Pro–Pro and the minimal promoter region of genes SOD and CAT using QCM-D and docking studies[J]. Analytical Methods, 2023, 15(24): 2979-2988.
[4] Song T, Lv M, Sun B, et al. Tripeptides Val-Pro-Pro (VPP) and Ile-Pro-Pro (IPP) regulate the proliferation and migration of vascular Smooth muscle cells by interfering Ang II-induced human umbilical vein endothelial cells derived EVs delivering RNAs to VSMCs in the co-culture model[J]. Journal of agricultural and food chemistry, 2020, 68(24): 6628-6637.
[5] Wang C, Zheng L, Zhao M. Molecular targets and mechanisms of casein-derived tripeptides Ile-Pro-Pro and Val-Pro-Pro on hepatic glucose metabolism[J]. Journal of Agricultural and Food Chemistry, 2023, 71(48): 18802-18814.
[6] Chakrabarti S, Wu J. Milk-derived tripeptides IPP (Ile-Pro-Pro) and VPP (Val-Pro-Pro) promote adipocyte differentiation and inhibit inflammation in 3T3-F442A cells[J]. PloS one, 2015, 10(2): e0117492.
[7] Nonaka A, Nakamura T, Hirota T, et al. The milk-derived peptides Val-Pro-Pro and Ile-Pro-Pro attenuate arterial dysfunction in L-NAME-treated rats[J]. Hypertension Research, 2014, 37(8): 703-707.
[8] Nakamura T, Hirota T, Mizushima K, et al. Milk-derived peptides, Val-Pro-Pro and Ile-Pro-Pro, attenuate atherosclerosis development in apolipoprotein E–deficient mice: a preliminary study[J]. Journal of medicinal food, 2013, 16(5): 396-403.

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