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产品名称：OMAPATRILAT
产品别名：奥马曲拉；BMS-186716

生物活性：

Description	Omapatrilat is a dual inhibitor of the metalloproteases ACE and NEP with Ki values of 0.64 and 0.45 nM, respectively.
IC_{50} & Target	Ki: 0.45 nM (NEP), 0.64 nM (ACE)[1]; IC50: 8 nM (NEP), 5 nM (ACE)[2]
In Vitro	Omapatrilat exhibits high potency for NEP, NEP2 and ACE, moderate strong activity against APP, but low activity against ECE1 (K_i=0.45, 25, 0.64, 250 nM) [1]. *In vitro* autoradiography using the specific NEP inhibitor radioligand 125I-RB104 and the specific ACE inhibitor radioligand 125I-MK351A show omapatril at (10 mg/kg) causes rapid and potent inhibition of renal NEP and ACE, respectively, for 24 h[4].
In Vivo	Omapatrilat demonstrates excellent blood pressure lowering in a variety of animal models characterized by various levels of plasma renin activity and significantly potentiates urinary sodium, ANP, and cGMP excretion in a cynomolgus monkey assay. Omapatrilat decreases mean arterial pressure (MAP) approximately 40 mmHg below baseline from 10 to 24 h. Oral administration of omapatrilat at 100 μM/kg once daily results in a 38 mmHg decrease in systolic blood pressure at day three as compared to vehicle [2]. Omapatrilat is widely used in experimental protocols related to hypertension and heart failure. Chronic oral administration of omapatrilat reduces aortic leakiness and atheroma formation with enhanced endothelial independent vasorelaxation to ANP[3]. Omapatrilat causes significant inhibition of plasma ACE and increased plasma renin activity in rats[4].
Solvent&Solubility	***In Vitro:*** **DMSO： ≥ 31 mg/mL (75.88 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4478 mL	12.2390 mL	24.4780 mL
	5 mM	0.4896 mL	2.4478 mL	4.8956 mL
	10 mM	0.2448 mL	1.2239 mL	2.4478 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

References

[1]. Fryer RM, et al. Effect of bradykinin metabolism inhibitors on evoked hypotension in rats: rank efficacy ofenzymes associated with bradykinin-mediated angioedema.Br J Pharmacol. 2008 Mar;153(5):947-55.

[2]. Robl JA, et al. Dual metalloprotease inhibitors: mercaptoacetyl-based fused heterocyclic dipeptide mimetics asinhibitors of angiotensin-converting enzyme and neutral endopeptidase. J Med Chem. 1997 May 23;40(11):1570-7.

[3]. Ichiki T, et al. Endothelial permeability in vitro and in vivo: protective actions of ANP and omapatrilat in experimental atherosclerosis. Peptides. 2013 Oct;48:21-6.

[4]. Burrell LM, et al. Antihypertensive and antihypertrophic effects of omapatrilat in SHR. Am J Hypertens.

	2000 Oct;13(10):1110-6.

实验参考：

Animal Administration	Rats: Sprague Dawley rats are weighed and then gavaged with vehicle (5% arabic gum) or omapatrilat (0.1, 1, 10 mg/kg) (n 5 6 rats/group). Rats are killed by decapitation at 1 h after gavage. Trunk blood is collected into prechilled tubes containing EDTA/aprotinin for the measurement of PRA and into prechilled heparin tubes for the measurement ofplasma ACE[4]. Rabbits: Omapatrilat is dissolved in drinking water. Rabbits are divided into 2 groups with 1% cholesterol diet, placebo-treated group and omapatrilat-treated group, and administrated (12 mg/Kg/day omapatrilat) once daily for 8 weeks. To demonstrate the acute effect of omapatrilat, urine is collected after omapatrilat or placebo administration for 24 hours at day 1, and urine volume, cGMP and ANP levels are assessed[3].
Kinase Assay	Omapatrilat is dissolved in 100% DMSO at 10 mM and diluted to 1% DMSO. NEP, NEP2, ACE and APP assays are performed at pH 7.4. The reaction buffer for NEP and NEP2 contained 50 mM HEPES, 140 mM NaCl, 10 mM KCl, 0.01% BSA. The buffer for ACE contained 100 mM Tris-HCl, 50 mM NaCl, 10 μM $ZnCl_2$, and the buffer for APP contained 100 mM HEPES and 0.01% BSA. Assays are performed in 100 μL volume in black 96-well round-bottom plates at room temperature. Reactions are continuously monitored with excitation and emission wavelengths appropriate for each respective substrate. Enzyme velocity is determined from the linear part of the reaction[1].
References	[1]. Fryer RM, et al. Effect of bradykinin metabolism inhibitors on evoked hypotension in rats: rank efficacy ofenzymes associated with bradykinin-mediated angioedema.Br J Pharmacol. 2008 Mar;153(5):947-55. [2]. Robl JA, et al. Dual metalloprotease inhibitors: mercaptoacetyl-based fused heterocyclic dipeptide mimetics asinhibitors of angiotensin-converting enzyme and neutral endopeptidase. J Med Chem. 1997 May 23;40(11):1570-7. [3]. Ichiki T, et al. Endothelial permeability in vitro and in vivo: protective actions of ANP and omapatrilat in experimental atherosclerosis. Peptides. 2013 Oct;48:21-6. [4]. Burrell LM, et al. Antihypertensive and antihypertrophic effects of omapatrilat in SHR. Am J Hypertens. 2000 Oct;13(10):1110-6.