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产品名称: **AHU-377**  
产品别名: 沙库必曲 ; **Sacubitril**

生物活性:

Description	Sacubitril (AHU-377) is a potent NEP inhibitor with an IC <sub>50</sub> of 5 nM. Sacubitril (AHU-377) is a component of the heart failure medicine LCZ696.				
IC <sub>50</sub> & Target	IC50: 5 nM (NEP) <sup>[1]</sup>				
In Vitro	Sacubitril (AHU-377) is a single molecule that is comprised of molecular moieties of valsartan, an ARB, and Sacubitril (AHU-377), a neprilysin inhibitor (1:1 ratio). Sacubitril (AHU-377) is converted by enzymatic cleavage of the ethyl ester into the active neprilysin inhibiting metabolite LBQ657 <sup>[2]</sup> . The inactive NEPi precursor, Sacubitril (AHU-377), does not inhibit collagen accumulation in fibroblasts nor cardiac myocyte hypertrophy. In cardiac fibroblasts, the active NEPi LBQ657 had no discernible effects. In contrast, LBQ657 modestly inhibits cardiac myocyte hypertrophy <sup>[3]</sup> .				
In Vivo	In humans, Sacubitril (AHU-377) (t <sub>max</sub> 0.5-1.1 h) are absorbed quickly. Sacubitril (AHU-377) is converted rapidly into LBQ657 with its t <sub>max</sub> being reached in 1.9-3.5 h. Mean t <sub>1/2</sub> values for the biologically active LBQ657 is 9.9-11.1 h <sup>[2]</sup> . In vehicle-treated dogs, ANF increases urinary sodium excretion from 17.3±3.6 to 199.5±18.4 pequivkg/min. This effect is potentiated significantly in animals which receive Sacubitril (AHU-377). Urinary volume is also potentiated in animals which receive an iv administration of Sacubitril (AHU-377) <sup>[1]</sup> .				
Solvent&Solubility	<b>In Vitro:</b>  DMSO : ≥ 100 mg/mL (243.02 mM)  H <sub>2</sub> O : < 0.1 mg/mL (insoluble)  * "≥" means soluble, but saturation unknown.				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	Preparing	1 mM	2.4302 mL	12.1510 mL	24.3019 mL
	Stock Solutions	5 mM	0.4860 mL	2.4302 mL	4.8604 mL
		10 mM	0.2430 mL	1.2151 mL	2.4302 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℃, 6 months; -20℃, 1 month。 -80℃ 储存时, 请在 6 个月内使用, -20℃ 储存时, 请在 1 个月内使用。				
	<b>In Vivo:</b>				
	请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液, 再依次添加助溶剂:				
	——为保证实验结果的可靠性, 澄清的储备液可以根据储存条件, 适当保存; 体内实验的工作液, 建议您现用现配, 当天使用; 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比; 如在配制过程中出现沉淀、析出现象, 可以通过加热和/或超声的方式助溶				
1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline					
Solubility: ≥ 2.5 mg/mL (6.08 mM); Clear solution					
此方案可获得 ≥ 2.5 mg/mL (6.08 mM, 饱和度未知) 的澄清溶液。					



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	<p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中, 混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80, 混合均匀; 然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2. 请依序添加每种溶剂: 10% DMSO <math>\rightarrow</math> 90% (20% SBE-<math>\beta</math>-CD in saline)</p> <p>Solubility: <math>\geq</math> 2.5 mg/mL (6.08 mM); Clear solution</p> <p>此方案可获得 <math>\geq</math> 2.5 mg/mL (6.08 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水水溶液中, 混合均匀。</p> <p>3. 请依序添加每种溶剂: 10% DMSO <math>\rightarrow</math> 90% corn oil</p> <p>Solubility: <math>\geq</math> 2.5 mg/mL (6.08 mM); Clear solution</p> <p>此方案可获得 <math>\geq</math> 2.5 mg/mL (6.08 mM, 饱和度未知) 的澄清溶液, 此方案不适用于实验周期在半个月以上的实验。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中, 混合均匀。</p>
References	<p>[1]. Ksander GM, et al. Dicarboxylic acid dipeptide neutral endopeptidase inhibitors. J Med Chem. 1995 May 12;38(10):1689-700.</p> <p>[2]. Voors AA, et al. The potential role of valsartan + AHU377 ( LCZ696 ) in the treatment of heart failure. Expert Opin Investig Drugs. 2013 Aug;22(8):1041-7.</p> <p>[3]. von Lueder TG, et al. Angiotensin receptor neprilysin inhibitor LCZ696 attenuates cardiac remodeling and dysfunction after myocardial infarction by reducing cardiac fibrosis and hypertrophy. Circ Heart Fail. 2015 Jan;8(1):71-8.</p>

源叶生物