Sacubitril

Cat. No.: HY-15407

CAS No.: 149709-62-6

Molecular Formula: $C_{24}H_{29}NO_5$

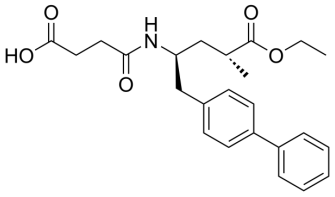
Molecular Weight: 411.49

Target: Neprilysin

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 75 mg/mL (182.26 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4302 mL	12.1510 mL	24.3019 mL
5 mM	0.4860 mL	2.4302 mL	4.8604 mL
10 mM	0.2430 mL	1.2151 mL	2.4302 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.08 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.08 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.08 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sacubitril (AHU-377) is a potent and orally active NEP (neprilysin) inhibitor with an IC_{50} of 5 nM. Sacubitril is a component of the heart failure medicine LCZ696. Sacubitril can be used for the research of heart failure, hypertension and COVID-19[1][2][3].

IC_{50} & Target

IC50: 5 nM (NEP)[1]

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[2]. 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[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In vehicle-treated dogs, ANF increases urinary sodium excretion from 17.3±3.6 to 199.5±18.4 pequivkglmin. 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)[1]. In normotensive rats, pretreatment with Sacubitril (3, 10 and 30 mg/kg, PO.) augments ANP-evoked plasma cGMP levels by 2.4, 3.3 and 4.0 fold, respectively (4h AUC compared to vehicle)[4]. Sacubitril (30 and 100 mg/kg, PO) produces a dose-dependent antihypertensive effect in Dahl-SS rats[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Theranostics. 2021; 11(18):8797-8812.

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REFERENCES

[1]. Hegde, L.G., et al. Comparative efficacy of AHU-377, a potent neprilysin inhibitor, in two rat models of volume-dependent hypertension. BMC Pharmacol 11, P33 (2011).

[2]. Ksander GM, et al. Dicarboxylic acid dipeptide neutral endopeptidase inhibitors. J Med Chem. 1995 May 12;38(10):1689-700.

[3]. 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.

[4]. 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.

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