Sacubitril hemicalcium salt

Cat. No.: HY-15407A

CAS No.: 1369773-39-6

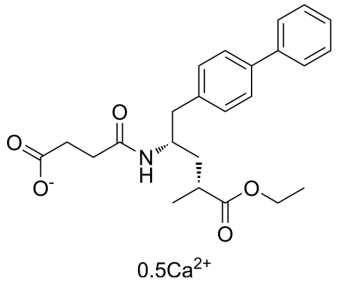
Molecular Formula: $C_{24}H_{28}Ca_{0.5}NO_5$

Molecular Weight: 430.52

Target: Neprilysin

Pathway: Metabolic Enzyme/Protease

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (290.35 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3228 mL	11.6139 mL	23.2277 mL
	5 mM	0.4646 mL	2.3228 mL	4.6455 mL
	10 mM	0.2323 mL	1.1614 mL	2.3228 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: ≥ 6.25 mg/mL (14.52 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 6.25 mg/mL (14.52 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 6.25 mg/mL (14.52 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sacubitril hemicalcium salt (AHU-377 hemicalcium salt) is a potent NEP inhibitor with an IC_{50} of 5 nM. Sacubitril hemicalcium salt is a component of the heart failure medicine LCZ696.

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 hemicalcium salt, 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 hemicalcium salt, 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 humans, Sacubitril (AHU-377)(t_{max} 0.5-1.1 h) are absorbed quickly. Sacubitril hemicalcium salt is converted rapidly into LBQ657 with its t_{max} being reached in 1.9-3.5 h. Mean $t_{1/2}$ values for the biologically active LBQ657 is 9.9-11.1 h[2].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]. 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]. Ksander GM, et al. Dicarboxylic acid dipeptide neutral endopeptidase inhibitors. J Med Chem. 1995 May 12;38(10):1689-700.

[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.

[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.

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