Sacubitril

Cat. No.: HY-15407
CAS No.: 149709-62-6
Molecular Formula: C₂₄H₂₉NO₅
Molecular Weight: 411.49
Target: Neprilysin
Pathway: Metabolic Enzyme/Protease
Storage:
- Powder: -20°C 3 years, 4°C 2 years
- In solvent: -80°C 6 months, -20°C 1 month

Solvent & Solubility

In Vitro
DMSO: ≥ 100 mg/mL (243.02 mM)
H₂O: < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.4302 mL</td>
<td>12.1510 mL</td>
<td>24.3019 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4860 mL</td>
<td>2.4302 mL</td>
<td>4.8604 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2430 mL</td>
<td>1.2151 mL</td>
<td>2.4302 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description
Sacubitril (AHU-377) is a potent NEP inhibitor with an IC₅₀ of 5 nM. Sacubitril (AHU-377) is a component of the heart failure medicine LCZ696.

IC₅₀ & Target
IC₅₀: 5 nM (NEP)
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].

In Vivo

In humans, Sacubitril (AHU-377) (t_{max} 0.5-1.1 h) are absorbed quickly. Sacubitril (AHU-377) 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 pequivkgmin. 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].

REFERENCES

