Sacubitril hemicalcium salt

Cat. No.: HY-15407A
CAS No.: 1369773-39-6
Molecular Formula: C₂₄H₂₈Ca₀.₅NO₅
Molecular Weight: 430.52
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 : 125 mg/mL (290.35 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.3228 mL</td>
<td>11.6139 mL</td>
<td>23.2277 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4646 mL</td>
<td>2.3228 mL</td>
<td>4.6455 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2323 mL</td>
<td>1.1614 mL</td>
<td>2.3228 mL</td>
<td></td>
</tr>
</tbody>
</table>

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 IC₅₀ of 5 nM. Sacubitril hemicalcium salt is a component of the heart failure medicine LCZ696.

IC₅₀ & 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].

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 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

