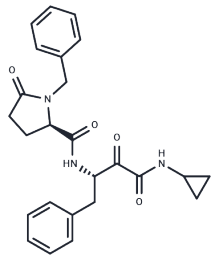
Data Sheet (Cat.No.T60150)

TargetMol

(1S,2R)-Alicapistat

Chemical Properties



CAS No. : 2221010-57-5

Formula: C25H27N3O4

Molecular Weight: 433.5

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	(1S,2R)-Alicapistat ((1S,2R)-ABT-957) is a highly efficient, orally active compound that selectively inhibits human calpains 1 and 2, showing promise for Alzheimer's disease (AD) therapy [1]. It effectively addresses the metabolic liability associated with carbonyl reduction and demonstrates potent inhibition of calpain 1 with an IC50 value of 395 nM [2].
Targets(IC50)	Proteasome,Cysteine Protease
In vitro	(1S,2R)-Alicapistat fails to achieve sufficient concentrations in the central nervous system (CNS) for a pharmacodynamic effect [1]. It inhibits Calpain 1 (μ-calpain) and 2 (m-calpain) in a calcium-dependent manner, requiring μ-molar or m-molar calcium concentrations for activation. At 100 nM, (1S,2R)-Alicapistat (compound 22) prevents deficits in synaptic transmission caused by Aβ oligomer in rats [2]. Furthermore, at 385 nM, it effectively prevents NMDA-induced neurodegeneration and amyloid beta (Aβ)-induced synaptic dysfunction [2]. At concentrations ranging from 9-21 nM in cerebrospinal fluid (CSF), (1S,2R)-Alicapistat does not reach the IC 50 required for calpain inhibition, yet it exhibits no dose-limiting toxicities (DLTs) across broad population studies [3].
In vivo	'(1S,2R)-Alicapistat (compound 22), administered intravenously (iv) or orally (po) at doses of 1-3 mg/kg, shows moderate plasma clearance rates (CLp) in mouse, rat, and dog (0.13-1.04 L/hr.kg) and higher rates in monkeys (1.98 L/hr.kg). The average steady-state volume of distribution (Vss) is moderate in mouse, dog, and monkey (0.64-1.8 L/kg), with rats displaying higher values (3.4 L/kg). The plasma elimination half-life (t 1/2) varies, being shortest in dogs (1.7 hours), 2.3 hours in monkeys, and approximately 6.0 hours in mice and rats. Oral bioavailability (F) is high in mice, rats, and dogs (>80%) but moderate in monkeys (14%) [2].'

Solubility Information

Solubility	DMSO: 45 mg/mL (103.81 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (2.31 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one.*

In vivo Formulation	*Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3068 mL	11.534 mL	23.0681 mL
5 mM	0.4614 mL	2.3068 mL	4.6136 mL
10 mM	0.2307 mL	1.1534 mL	2.3068 mL
50 mM	0.0461 mL	0.2307 mL	0.4614 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Lon HK, et al. Pharmacokinetics, Safety, Tolerability, and Pharmacodynamics of Alicapistat, a Selective Inhibitor of Human Calpains 1 and 2 for the Treatment of Alzheimer Disease: An Overview of Phase 1 Studies. Clin Pharmacol Drug Dev. 2019 Apr. 8(3):290.

Jantos K, et al. Discovery of ABT-957: 1-Benzyl-5-oxopyrrolidine-2-carboxamides as selective calpain inhibitors with enhanced metabolic stability. Bioorg Med Chem Lett. 2019 Aug 1. 29(15):1968-1973.

Jastaniah A, Gaisina IN, Knopp RC, Thatcher GRJ. Synthesis of α-Ketoamide-Based Stereoselective Calpain-1 Inhibitors as Neuroprotective Agents. ChemMedChem. 2020 Dec 3. 15(23):2280-2285.