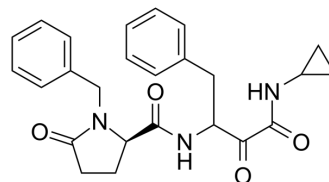


Alicapistat

Cat. No.:	HY-109001		
CAS No.:	1254698-46-8		
Molecular Formula:	C ₂₅ H ₂₇ N ₃ O ₄		
Molecular Weight:	433.5		
Target:	Proteasome		
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 : 50 mg/mL (115.34 mM; ultrasonic and warming and heat to 60°C)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	Preparing Stock Solutions	1 mM	2.3068 mL	11.5340 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	
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: ≥ 4.17 mg/mL (9.62 mM); Clear solution 2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (5.77 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	Alicapistat (ABT-957) is an orally active selective inhibitor of human calpains 1 and 2 for the potential application of Alzheimer's disease (AD) ^[1] . Alicapistat mitigates the metabolic liability of carbonyl reduction and inhibits calpain 1 with an IC ₅₀ value of 395 nM ^[2] .
IC₅₀ & Target	IC ₅₀ : 395 nM (Human calpains 1) ^[2] .
In Vitro	Alicapistat exhibits inadequate CNS-penetration concentrations to obtain a pharmacodynamic effect ^[1] . Calpain 1 (μ-calpain) and 2 (m-calpain) expression in a calcium-dependent manner with μ-molar or m-molar calcium concentrations required for their respective activation, respectively. Alicapistat (compound 22) (100 nM) prevents Aβ oligomer-induced deficits in synaptic transmission in rat ^[2] .

Alicapostat (compound 22) (385 nM) displays efficacy with respect to prevention of NMDA-induced neurodegeneration and A-induced synaptic dysfunction in rat hippocampal slice cultures^[2].

Alicapostat (9-21 nM) has the CSF concentrations without reaching the IC₅₀ for calpain inhibition and shows no dose-limiting toxicities (DLTs) in the broad populations studies^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Alicapostat (compound 22) (iv or po; 1-3 mg/kg) shows moderate mean plasma clearance values (CL_p) in mouse, rat, and dog (0.13-1.04 L/hr.kg), while high in monkey (1.98 L/hr.kg). Mean steady-state volume of distribution values (V_{ss}) were moderate in mouse, dog, and monkey (0.64-1.8 L/kg), but higher in rat (3.4 L/kg). The plasma elimination half-life (t_{1/2}) was shortest in dog (1.7 hours), followed by 2.3 hours in monkey and approximately 6.0 hours in mouse and rat. Oral bioavailability (F) values were high in mouse, rat, and dog (>80%), while moderate in monkey (14%)^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Rep. 2021 Jun 24;11(1):13208.

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REFERENCES

[1]. 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.

[2]. 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.

[3]. Lon HK, et al. Pharmacokinetics, Safety, Tolerability, and Pharmacodynamics of Alicapostat, 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.* 2018 Jul 27.

Caution: Product has not been fully validated for medical applications. For research use only.

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