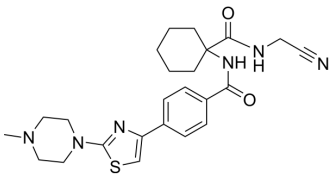
L-006235

Cat. No.:	HY-103352
CAS No.:	294623-49-7
Molecular Formula:	$C_{24}H_{30}N_6O_2S$
Molecular Weight:	466.6
Target:	Cathepsin
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 : 31.25 mg/mL (66.97 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1432 mL	10.7158 mL	21.4316 mL
	5 mM	0.4286 mL	2.1432 mL	4.2863 mL
	10 mM	0.2143 mL	1.0716 mL	2.1432 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: ≥ 2.08 mg/mL (4.46 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.46 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.46 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

L-006235 (L-235) is a potent, selective, reversible and orally active inhibitor of cathepsin K, with an IC_{50} of 5 nM in bone resorption assay. L-006235 shows selectivity for cathepsin K (K_i=0.2 nM) over cathepsin B, cathepsin L, and cathepsin S (K_i=1, 6, and 47 μM, respectively). L-006235 can reduce collagen degradation and prevent bone loss[1][2].

IC_{50} & Target		
	Cathepsin B	cathepsin K

In Vitro

L-006235 inhibits bone resorption in the rabbit bone resorption assay, with an IC_{50} of 5 nM[1].

L-006235 (10 μM; 1 h) show a punctate fluorescence throughout the cytoplasm in HepG2 cells[2].

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

In Vivo

L-006235 (0.6-15 mg/kg; p.o. qd for 8-11 d) reduces N-telopeptides (NTx) and creatinine (Cre) by up to 76% dose-dependently in rhesus monkey[1].

L-006235 (20 mg/kg; p.o.) exhibits high oral bioavailability (68%), long terminal half-life (204 min) and C_{max} (1.4 μM) in rats[1].

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

Animal Model:	Rhesus monkey (15 years) receiving oophorectomy (OVX)[1]
Dosage:	0.6, 3, 15 mg/kg
Administration:	P.o once daily for 8-11 days
Result:	Decreased uNTx/Cre by an average of 76%, 68%, and 31% at the dose of 15, 3, and 0.6 mg/kg, respectively.

REFERENCES

[1]. Palmer JT, et, al. Design and synthesis of tri-ring P3 benzamide-containing aminonitriles as potent, selective, orally effective inhibitors of cathepsin K. J Med Chem. 2005 Dec 1;48(24):7520-34.

[2]. Falgueyret JP, et, al. Lysosomotropism of basic cathepsin K inhibitors contributes to increased cellular potencies against off-target cathepsins and reduced functional selectivity. J Med Chem. 2005 Dec 1;48(24):7535-43.

[3]. Pennypacker BL, et, al. Cathepsin K inhibitors prevent bone loss in estrogen-deficient rabbits. J Bone Miner Res. 2011 Feb;26(2):252-62.

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