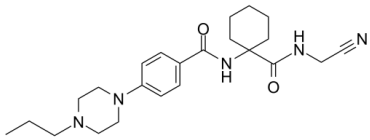
Data Sheet

Product Name:	Balicatib
Cat. No.:	CS-2623
CAS No.:	354813-19-7
Molecular Formula:	C23H33N5O2
Molecular Weight:	411.54
Target:	Cathepsin
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 46 mg/mL (111.78 mM)



BIOLOGICAL ACTIVITY:

Balicatib(AAE-581) is a potent and selective inhibitor of cathepsin K; 10-100 fold more potent in cell-based enzyme occupancy assays than against cathepsin B, L, and S. IC50 value: Target: cathepsin K The cathepsin K inhibitor AAE-581 (balicatib) as the most advanced of them passed Phase II clinical trials in 2005. Eighty adult female Macaca fascicularis underwent bilateral ovariectomies and were dosed twice daily by oral gavage with balicatib at 0, 3, 10, and 50 mg/kg for 18 months (groups O, L, M, H, respectively). Approximately 1 month after treatment initiation, the 50 mg/kg dose was decreased to 30 mg/kg. Twenty animals underwent sham-ovariectomies (group S). Bone mass was measured at 3-6 month intervals. At 18 months, vertebra and femur were collected for histomorphometry.

PROTOCOL (Extracted from published papers and Only for reference)

Animal administration [3] A total of 105 purpose-bred, female cynomolgus monkeys (Macaca fascicularis) aged 11-13 years are acclimated and monitored daily for signs of ill health for approximately 1 month prior to surgery. Balicatib or vehicle (sterile water) is administered orally twice daily by nasogastric intubation, starting the day after ovariectomy or sham surgery. Balicatib is dissolved in sterile water to achieve the appropriate high dose concentration (50 or 30 mg/kg/day), and serial dilutions are prepared to achieve the correct concentrations for the middle- (10 mg/kg/day) and low-dose (3 mg/kg/day) solutions. Dose solutions are prepared weekly and refrigerated until day of use. Following the reduction of the high dose, the pH of the high dose solution is adjusted to 6.5 using NaOH.

References:

[1]. 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.

[2]. Vasiljeva O, et al. Emerging roles of cysteine cathepsins in disease and their potential as drug targets. Curr Pharm Des. 2007;13(4):387-403.

[3]. Jerome C, et al. Balicatib, a cathepsin K inhibitor, stimulates periosteal bone formation in monkeys. Osteoporos Int. 2011 Dec;22(12):3001-11.

CAIndexNames:

Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)-

SMILES:

CCCN1CCN(C2=CC=C(C(NC3(C(NCC#N)=O)CCCCC3)=O)C=C2)CC1

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

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