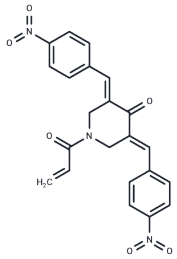
Data Sheet (Cat.No.T1932)

TargetMol

B-AP15

Chemical Properties



CAS No. : 1009817-63-3

Formula: C22H17N3O6

Molecular Weight: 419.39

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	B-AP15 (NSC-687852)(NSC-687852) is a selective inhibitor of the deubiquitinating enzymes Usp14 and UCHL5 of the 26S proteasome. It blocks the deubiquitinating activity of the 26S proteasome.
Targets(IC50)	Apoptosis,DUB
In vitro	In mice with HCT-116 colon carcinoma xenografts, B-AP15 (5 mg/kg) significantly delayed tumor onset. Additionally, in severely immunodeficient mice bearing squamous cell carcinoma xenografts, B-AP15 (5 mg/kg) demonstrated notable antitumor activity.
In vivo	As a UPS (Ubiquitin-Proteasome System) inhibitor, B-AP15 induces cell death by triggering the cathepsin-D-dependent lysosomal apoptotic pathway. Compared to peripheral blood mononuclear cells or immortalized epithelial cells (hTERT-RPE1), B-AP15 exhibits greater cytotoxicity towards HCT-116 cells. It dose-dependently accumulates the UbG76V-YFP receptor (IC50: 0.8 μM), indicating impaired proteasomal degradation. When applied to human colon cancer HCT-116 cells, B-AP15 (1 μM) rapidly accumulates polyubiquitinated proteins. At a concentration of 1 μM, B-AP15 inhibits the release of IL-1β induced by ATP from lipopolysaccharide-induced peritoneal macrophages. In THP-1 cells, 1 μM B-AP15 reduces the level of cell death induced by nigericin and significantly decreases the formation of ASC specks in lipopolysaccharide-induced THP-1 cells treated with nigericin. Additionally, B-AP15 (1 μM) causes a G2/M phase cell cycle arrest and accumulation of cell cycle inhibitors in HCT-116 cells. At 2.2 μM, B-AP15 dose-dependently increases the levels of the cyclin-dependent kinase inhibitors CDKN1A and CDKN1B, and the tumor suppressor gene TP53, without affecting the levels of ornithine decarboxylase 1.
Kinase Assay	For deubiquitinase inhibition assays, 19S regulatory particle (5 nM), 26S (5 nM) UCH-L1 (5 nM), UCH-L3 (0.3 nM), USP2CD (5 nM) USP7CD (5 nM) USP8CD (5 nM) or BAP1 (5 nM) is incubated with DMSO or b-AP15 and monitored the cleavage of ubiquitin-AMC (1,000 nM) using a Wallac VICTOR Multilabel counter or a Tecan Infinite M1000 equipped with 380 nm excitation and 460 nm emission filters[1].
Cell Research	b-AP15 is dissolved in DMSO and stored, and then diluted with appropriate medium before use[2]. Cell viability is monitored by either the fluorometric microculture cytotoxicity assay or the MTT assay. For the MTT assay, cells are seeded into 96-well flat-bottomed plates overnight and exposed to drugs, using DMSO as the control. At the end of incubations, 10 μl of a stock solution of 5 mg/mL MTT is added into each well, and the plates are incubated 4 hours at 37°C. Formazan crystals are dissolved with 100 μL 10%

	SDS/10 mM HCl solution overnight at 37°C. Absorbance is measured using an enzyme-linked immunosorbent assay (ELISA) plate reader at 590 nm[2].

Solubility Information

Solubility	DMSO: 1 mg/mL (2.38 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3844 mL	11.9221 mL	23.8442 mL
5 mM	0.4769 mL	2.3844 mL	4.7688 mL
10 mM	0.2384 mL	1.1922 mL	2.3844 mL
50 mM	0.0477 mL	0.2384 mL	0.4769 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.

Reference

D'Arcy P, et al. Nat Med. 2011, 17(12):1636-40.
Wu W, Xu H, Liao C, et al. Blockade of USP14 potentiates type I interferon signaling and radiation-induced antitumor immunity via preventing IRF3 deubiquitination. Cellular Oncology. 2022: 1-15
Yue X, Liu T, Wang X, et al.Pharmacological inhibition of BAP1 recruits HERC2 to competitively dissociate BRCA1-BARD1, suppresses DNA repair and sensitizes CRC to radiotherapy.Acta Pharmaceutica Sinica B.2023
D'Arcy P, et al. Int J Biochem Cell Biol. 2012, 44(11):1729-38.
Lopez-Castejon G, et al. J Biol Chem, 2013, 288(4), 2721-2733.