Product Data Sheet

Product Name: BV6
Cat. No.: GC12333

Chemical Properties

Cas. No.	1001600-56-1
Chemical Name	(S,S,2S,2'S)-N,N'-((2S,2'S)-(hexane-1,6-diylbis(azanediyl))bis(3-oxo-1,1-diphenylpropane-3,2-diyl))bis(1-((S)-2-cyclohexyl-2-((S)-2-(methylamino)propanamido)acetyl)pyrrolidine-2-carboxamide)
SMILES	O=C(CCCCCCCNC([C@@H](NC([C@H]1N(C([C@H](C2CCCCC2)NC([C@H](C)NC)=O)=O)CCC1)=O)CO=C(NCCCCCCCNC([C@@H](NC([C@H]1N(C([C@H](C2CCCCC2)NC([C@H](C)NC)=O)=O)CCC1)=O)C(C3=CC=CC=C3)C4=CC=CC=C4)=O)[C@@H](NC([C@H]5N(C([C@H](C6CCCCC6)NC([C@H](C)NC)=O)=O)CCC5)=O)C(C7=CC=
Formula	$C_{70}H_{96}N_{10}O_8$
M.Wt	1205.57
Solubility	≥ 60.2785mg/mL in DMSO
Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.
Structure	BV6

Protocol

Cell experiment [1]:

Cell lines	HCC193 and H460 non-small cell lung cancer (NSCLC) cell lines.

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Preparation method	Limited solubility. General tips for obtaining a higher concentration: Please warm the tube at 37 ℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reaction Conditions	37℃
Applications	BV6 reduces the expression of cIAP1 and XIAP in HCC193 and H460 cell lines in a time and dose-dependent manner. BV6 also induces apoptosis in both HCC193 and H460 cell lines. In addition, BV6 prominently promotes the radiosensitivity of both HCC193 and H460 lung cancer cell lines.

Animal experiment [2]:

Animal models	Mouse endometriosis model
Dosage form	Single i.p. injection of BV6 (10 mg/kg) twice weekly.
Applications	BV6 treatment for 4 weeks attenuates the intensity of IAPs expression and lowers the total number of lesions, the average weight and the surface area of lesions as compared with control group. Moreover, BV6 treatment decreases the percentage of Ki67-positive cells in the endometrial gland epithelia or stroma.

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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

1. Li W, Li B, Giacalone NJ, Torossian A et al. BV6, an IAP antagonist, activates apoptosis and enhances radiosensitization of non-small cell lung carcinoma in vitro. J Thorac Oncol. 2011 Nov;6(11):1801-9.

2. Uegaki T, Taniguchi F, Nakamura K et al. Inhibitor of apoptosis proteins (IAPs) may be effective therapeutic targets for treating endometriosis. Hum Reprod. 2015 Jan;30(1):149-58.

Background

BV6 is a selective inhibitor of IAP family with IC50 value of 7.2 μM when tested with H460 cells [1].
IAP (inhibitor of apoptosis) is a family protein consists of 8 members and serves as endogenous inhibitors of programmed cell death. Until now, more than 5 human IAPs have been discovered includes XIAP, c-IAP1, c-IAP-2, NAIP, Livin and Survivin. It is reported that IAPs overexpression protects cells against a number of proapoptotic stimuli which enables IAPs play a pivotal role in promoting cancer cell survival [2, 3]. BV6 is an inhibitor of IAP family and often used as an adjuvant to sensitize the cancer cells to radiotherapy or chemotherapy. When tested with H460 NSCLC cells, pre-treatment BV6 sensitized the cells to radiation and increased the apoptosis in a time-

and dose- dependent manner via reducing the expression of cIAP1 and XIAP [1]. In hematological THP-1 cells, pre-treatment with BV6 increased the CIK cells killing ability and the same results were achieved in solid malignancy RH30 cells [4]
In BALB/c mice model with transplanted abdominal cavities from donor mouse uterine tissue, intraperitoneally with BV6 repressed the advancement of endometriosis, cell proliferative activity via inhibiting the expression of IAPs [5].

References:

[1]. Li, W., et al., BV6, an IAP antagonist, activates apoptosis and enhances radiosensitization of non-small cell lung carcinoma in vitro. J Thorac Oncol, 2011. 6(11): p. 1801-9.

[2]. Altieri, D.C., Survivin - The inconvenient IAP. Semin Cell Dev Biol, 2015.

[3]. Fulda, S., Smac mimetics as IAP antagonists. Semin Cell Dev Biol, 2014.

[4]. Rettinger, E., et al., SMAC Mimetic BV6 Enables Sensitization of Resistant Tumor Cells but also Affects Cytokine-Induced Killer (CIK) Cells: A Potential Challenge for Combination Therapy. Front Pediatr, 2014. 2: p. 75.

[5]. Uegaki, T., et al., Inhibitor of apoptosis proteins (IAPs) may be effective therapeutic targets for treating endometriosis. Hum Reprod, 2015. 30(1): p. 149-58.