

Product Data Sheet

Product Name: Epoxomicin

Cat. No.: GC12494

Chemical Properties

Cas. No. 134381-21-8

Chemical Name (2S,3S)-2-[[[(2S,3S)-2-[acetyl(methyl)amino]-3-methylpentanoyl]amino]-N-[(2S,3R)-3-hydroxy-1-[[[(2S)-4-methyl-1-[(2R)-2-methyloxiran-2-yl]-1-oxopentan-2-yl]amino]-1-oxobutan-2-yl]-3-methylpentanamide

SMILES CCC(C)C(C(=O)NC(C(C)O)C(=O)NC(CC(C)C)C(=O)C1(CO1)C)NC(=O)C(C(C)CC)N(C)C(=O)C

Formula C₂₈H₅₀N₄O₇

M.Wt 554.7

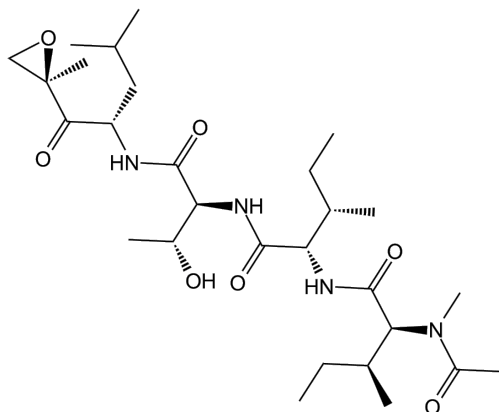
Solubility ≥ 27.74mg/mL in DMSO

Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

Cell experiment [1]:

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Cell lines	HEK293T cells
Preparation method	HEK293T cells were grown to 90% confluence. At the start of the experiment, media were removed from all plates and media with or without epoxomicin were placed into the plates incubated at 37°C for 1h. Two concentrations of epoxomicin were used, 0.2 and 2µM, prepared by a 1:2500 dilution of 0.5 and 5 mM solutions of epoxomicin in DMSO, respectively.
Reaction Conditions	0.2 and 2µM; 1 h
Applications	Peptides are degraded from cytoplasmic, mitochondrial and nuclear proteins by proteasomes. Epoxomicin inhibits proteasome beta-2 and beta-5 subunits in HEK293T cells.
Animal experiment [2]:	
Animal models	C57BL/6 mice
Preparation method	mice were weighed and injected intraperitoneally with vehicle or epoxomicin , 0.5mg/kg. One hour after the first injection, animals were injected with vehicle or LPS, 7.5 mg/kg. Mice were anesthetized eight hours after LPS administration with a lethal injection of a mix of ketamine and xylazine. Measuring all three β1, β2 and β5 activities of the 20S and 26S proteasomes, the levels of steady state polyubiquitinated proteins.

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Dosage form	0.5mg/kg; i.p.
Applications	Epoxomicin decreased polyubiquitination by 23% in GAS muscle and conversely increased it by 41% in liver, the latter being consistent with proteasome $\beta 5$ inhibition.
References: [1] Fricker L D, Gelman J S, Castro L M, et al. Peptidomic analysis of HEK293T cells: effect of the proteasome inhibitor epoxomicin on intracellular peptides[J]. Journal of proteome research, 2012, 11(3): 1981-1990. [2] Jamart, Cécile, Gomes A V , Dewey S ,et al. Regulation of ubiquitin-proteasome and autophagy pathways after acute LPS and epoxomicin administration in mice[J].Bmc Musculoskeletal Disorders, 2014, 15(1):166.	

Background

Epoxomicin is a selective proteasome inhibitor that effectively inhibits the chymotrypsin-like (CH-L) activity of the 20S proteasome, with an IC_{50} of approximately 40-80nM^[1]. Epoxomicin covalently binds to the catalytic β subunits LMP 7, X, Z, and MECL 1 of the proteasome, leading to inhibition of the proteasome subunits' CH-L, T-L, and PGPH catalytic activities^[2].

In vitro, Epoxomicin shows considerable cytotoxicity against B16-F10, HCT116, Moser, P388, and K562 cells, with IC_{50} values of 0.002 μ g/mL, 0.005 μ g/mL, 0.044 μ g/mL, 0.002 μ g/mL, and 0.037 μ g/mL, respectively^[3]. Epoxymycin (0.2 and 2 μ M) treated HEK293T cells for 1 hour, inhibiting the expression of proteasome beta-2 and beta-5 subunits in the cells^[4]. Epoxomicin (100 nM) for 24 hours in Plasmodium falciparum cells results in a 77% reduction in gametocytes^[5].

In vivo, Epoxymycin (0.5mg/kg), administered intraperitoneally, reduced polyubiquitination in GAS muscle of C57BL/6 mice by 23% and increased polyubiquitination in liver by 41%, the latter associated with The inhibitory effect of proteasome $\beta 5$ is consistent ^[6]. Epoxymycin (0.5mg/kg/day)

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was administered to KI and WT mice for 1 week using a subcutaneously implanted osmotic minipump, which reduced the chymotrypsin-like activity of the mice by approximately 50%^[7].

References:

- [1] Meng L , Mohan R , Kwok B H B ,et al.Epoxomicin, a potent and selective proteasome inhibitor, exhibits in vivo antiinflammatory activity[J]. Proceedings of the National Academy of Sciences, 1999, 96(18):10403-10408.
- [2] Aboulaila M , Nakamura K , Govind Y ,et al.Evaluation of the in vitro growth-inhibitory effect of epoxomicin on Babesia parasites.[J].Veterinary Parasitology, 2010, 167(1):19-27.
- [3] Hanada M, Sugawara K, Kaneta K, et al. Epoxomicin, a new antitumor agent of microbial origin. [J] Antibiot (Tokyo). 1992 Nov;45(11):1746-52.
- [4] Fricker L D, Gelman J S, Castro L M, et al. Peptidomic analysis of HEK293T cells: effect of the proteasome inhibitor epoxomicin on intracellular peptides[J]. Journal of proteome research, 2012, 11(3): 1981-1990.
- [5] Czesny B , Goshu S , Cook J L ,et al. The Proteasome Inhibitor Epoxomicin Has Potent Gametocytocidal Activity[J]. 2009.
- [6]Jamart, Cécile, Gomes A V , Dewey S ,et al. Regulation of ubiquitin-proteasome and autophagy pathways after acute LPS and epoxomicin administration in mice[J].Bmc Musculoskeletal Disorders, 2014, 15(1):166.
- [7]Schlossarek,Saskia,Singh,et al. Proteasome inhibition slightly improves cardiac function in mice with hypertrophic cardiomyopathy[J].Frontiers in Physiology, 2014.

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