

Product Data Sheet

Product Name: Actinonin

Cat. No.: GC16350

Chemical Properties

Cas. No. 13434-13-4

Chemical Name (2R)-N4-hydroxy-N1-[(1S)-1-[[[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]carbonyl]-2-methylpropyl]-2-pentyl-butanediamide

SMILES O=C([C@H](C(C)C)NC([C@H](CCCC)CC(NO)=O)=O)N1CCC[C@H]1CO

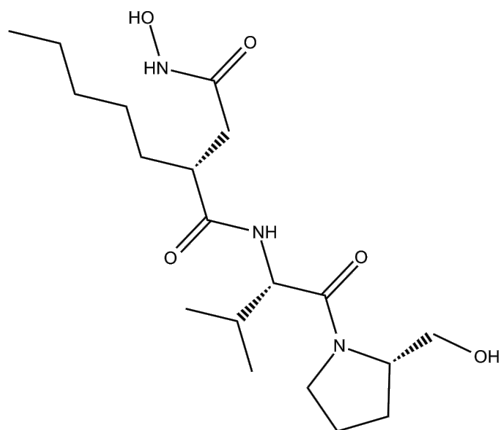
Formula $C_{19}H_{35}N_3O_5$ M.Wt 385.5

Solubility 30mg/ml in ethanol;30mg/ml in DMSO;30mg/ml in dimethyl formamide 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 U937 cells

Preparation Method The U937 cells were suspended in RPMI 1640 medium containing 10% fetal bovine serum (FBS) and 2mM glutamine at a final concentration of 1.5×10^5 cells/ml, and then inoculated into 24-well culture plates. Subsequently, different concentrations of Actinonin (2.5, 5, 10, and 20µg/ml) were added to each well, and the culture plates were placed in a humidified incubator at 37°C and 5% CO₂ for 72h. The cells were counted every day and stained with trypan blue.

Reaction Conditions 2.5, 5, 10, and 20µg/ml; 72h

Applications Actinonin treatment inhibited the proliferation and viability of U937 cells in a concentration-dependent manner.

Animal experiment [2]:

Animal models Athymic NCr-nu mice

Preparation Method Subcutaneously inoculate A549 cells (5×10^6) on the lateral abdomen of 8 to 10-week-old athymic NCr-nu mice. Once the tumors can be felt, the mice were randomly divided into a control group and a treatment group, with 3-5 mice in each group. The control group was given a vehicle intraperitoneally and the treatment group was intraperitoneal injection of 150mg/kg of Actinonin, once a day, for 2 weeks. The tumor size was measured with a vernier caliper every 3-4 days.

Dosage form 150mg/kg/day for 2 weeks; i.p.

Applications Actinonin treatment significantly reduced tumor growth in the A549 cell-xenograft mouse model.

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References:

- [1] Grujic M, Zavasnik-Bergant T, Pejler G, et al. Actinonin induces apoptosis in U937 leukemia cells[J]. Cancer letters, 2005, 223(2): 211-218.
- [2] Lee M D, She Y, Soskis M J, et al. Human mitochondrial peptide deformylase, a new anticancer target of actinonin-based antibiotics[J]. The Journal of clinical investigation, 2004, 114(8): 1107-1116.

Background

Actinonin, a peptidomimetic antibiotic that inhibits enkephalin-aminopeptidase, enkephalinase A, and dipeptidylaminopeptidase with IC₅₀ values of 0.39μM, 5.6μM, and 1.1μM, respectively^[1]. Actinonin can inhibit the constitutive expression of functional recombinant MT1-MMP protein, block the activation of proMMP-2, and suppress angiogenesis^[2]. Actinonin has been widely used as an antibacterial agent to inhibit the growth of Gram-positive bacteria and difficult-to-culture Gram-negative bacteria^[3].

In vitro, Actinonin treatment for 5 days significantly inhibited the viability of HL-60 cells, NB4 cells and AKR cells with IC₅₀ values of 2μg/ml, 5μg/ml, and 3μg/ml, respectively^[4]. Treatment of U937 cells with 20μg/ml of Actinonin for 24 hours significantly induced cell apoptosis, accompanied by a significant increase in the activities of caspase-3 and caspase-7-like enzymes and extensive fragmentation of DNA^[5]. Actinonin pretreatment at 26nM for 1 hour can reduce the expression of HSP70 induced by celastrol in U937 cells, and synergistically inhibit cell proliferation with celastrol^[6].

In vivo, Actinonin treatment via daily intraperitoneal injection (150mg/kg/day) for 2 weeks significantly inhibited tumor growth in the A549 xenograft mouse model without causing any toxic reactions^[7]. Thirty minutes before the mice underwent cecal ligation and puncture (CLP), a single dose of Actinonin (20mg/kg) was injected intraperitoneally, which could reduce the serum IL-1β level and prevent the decline in renal capillary perfusion^[8].

References:

- [1] Hachisu M, Hiranuma T, Murata S, et al. Analgesic effect of actinonin, a new potent inhibitor of multiple enkephalin degrading enzymes[J]. Life sciences, 1987, 41(2): 235-240.

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- [2] Sina A, Lord-Dufour S, Annabi B. Cell-based evidence for aminopeptidase N/CD13 inhibitor actinonin targeting of MT1-MMP-mediated proMMP-2 activation[J]. Cancer letters, 2009, 279(2): 171-176.
- [3] Chen D Z, Patel D V, Hackbarth C J, et al. Actinonin, a naturally occurring antibacterial agent, is a potent deformylase inhibitor[J]. Biochemistry, 2000, 39(6): 1256-1262.
- [4] Xu Y, Lai L T, Gabrilove J L, et al. Antitumor activity of actinonin in vitro and in vivo[J]. Clinical cancer research: an official journal of the American Association for Cancer Research, 1998, 4(1): 171-176.
- [5] Grujic M, Zavasnik-Bergant T, Pejler G, et al. Actinonin induces apoptosis in U937 leukemia cells[J]. Cancer letters, 2005, 223(2): 211-218.
- [6] Peng B, Zhang X, Cao F, et al. Peptide deformylase inhibitor actinonin reduces celastrol's HSP70 induction while synergizing proliferation inhibition in tumor cells[J]. BMC Cancer, 2014, 14(1): 146.
- [7] Lee M D, She Y, Soskis M J, et al. Human mitochondrial peptide deformylase, a new anticancer target of actinonin-based antibiotics[J]. The Journal of clinical investigation, 2004, 114(8): 1107-1116.
- [8] Wang Z, Herzog C, Kaushal G P, et al. Actinonin, a meprin A inhibitor, protects the renal microcirculation during sepsis[J]. Shock, 2011, 35(2): 141-147.

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