

Product Data Sheet

Product Name: Pentostatin

Cat. No.: GC12200

Chemical Properties

Cas. No. 53910-25-1

Chemical Name (8R)-3-[(2R,4S,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-7,8-dihydro-4H-imidazo[4,5-d][1,3]diazepin-8-ol

SMILES C1C(C(OC1N2C=NC3=C2NC=NCC3O)CO)O

Formula $C_{11}H_{16}N_4O_4$ M.Wt 268.27

Solubility ≥ 13.4 mg/mL in DMSO, ≥ 26.8 mg/mL in Water 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.

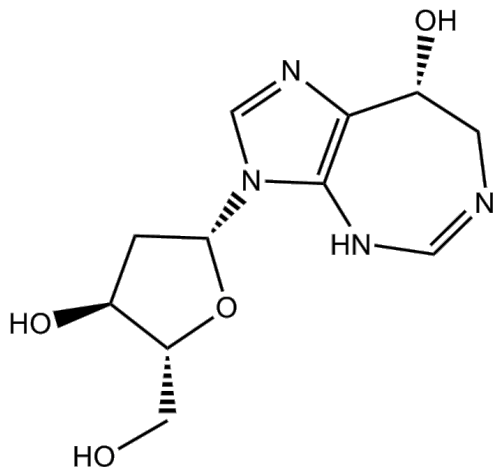
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Structure



Protocol

Kinase experiment [1]:

Fresh dilutions of Pentostatin (0.005, 0.05, 0.125, 0.5, 5, 12.5, 50, 125, 500, 1000 μ M) in phosphate buffer were prepared. 30 μ L of 13.8mUmL⁻¹ adenosine deaminase (ADA) and 20 μ L of Pentostatin were added to successive wells in a Preparation Method row and thoroughly mixed. In the final two wells of the row, phosphate buffer and EHNA were added, respectively, in place of Pentostatin. Two more rows were prepared in the same manner and a fourth row was prepared with phosphate buffer in place of ADA.

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Reaction Conditions After two minutes of incubation, isothiazolo adenosine (^tzA) (50μL of 7.8μM) was added and mixed thoroughly. Wells were then excited at 322nm and emission monitored at 410nm. Intensity of emission was measured every 37 seconds for just over 30 minutes.

Applications The IC₅₀ value of Pentostatin is 0.0014±0.0001μM, and K_i value is 0.0012±0.0002μM

Cell experiment [2]:

Cell lines human Primary Lymphocytes

Preparation Method Freeze dried Pentostatin was reconstituted with PBS, resterilized by filtration and added to cultures by pipetting on to the surface of the agar. Control cultures received the same volume of saline. Pilot experiments showed that Pentostatin was much less effective when incorporated into the agar underlay than when pipetted on to the surface. Application of Pentostatin to the agar surface had the further advantage that it could be done at any time after setting up the culture. It is however difficult to be precise about drug concentrations reaching cells by diffusion through soft agar. Cited concentrations are those pipetted on to the agar surface and are therefore all over-estimates by up to 10-fold of the concentrations surrounding the cells, since the volume of saline in which the Pentostatin was applied was one tenth that of the agar in each well.

Reaction Conditions 100μM-1nM; 4h

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Applications T cells already proliferating in response to PHA are less sensitive to Pentostatin, implying that S-phase events are not primary targets of the drug's action. Colony inhibition does not appear to be due to alteration in the production of, or sensitivity to, soluble T cell growth factors. In suspension cultures, Pentostatin at concentrations up to 100µM fails to inhibit early PHA-induced volume changes, or later mitosis, in peripheral blood lymphocytes.

Animal experiment [3]:

Animal models C57BL/6 nude mice

Preparation Method Mice were implanted subcutaneously with CT26/NY-ESO-1 cells and received 10µg of intravenous Pentostatin alone ("Pentostatin") or together with 1mg intraperitoneally of an anti-IFNAR antibody ("Pentostatin + anti-IFNAR ab") 6 days later. As controls, tumor-bearing mice received only the anti-IFNAR ab ("anti-IFNAR ab") or were left untreated ("Untreated") at day 6.

Dosage form 10µg; once; i.v

Applications Pentostatin can be used to treat CT26/NY-ESO-1 tumors, but its activity is abrogated by anti-IFNAR ab

References:

[1]Adamek, Rebecca N et al. "Identification of Adenosine Deaminase Inhibitors by Metal-binding Pharmacophore Screening." *ChemMedChem* vol. 15,22 (2020): 2151-2156.

doi:10.1002/cmdc.202000271

[2]Colledge, N R et al. "Action of deoxycoformycin on human T cell colonies in vitro." *Clinical and experimental immunology* vol. 50,1 (1982): 115-22.

[3]Tusup, Marina et al. "Epitranscriptomics modifier pentostatin indirectly triggers Toll-like receptor 3 and can enhance immune infiltration in tumors." *Molecular therapy : the journal of the American Society of Gene Therapy* vol. 30,3 (2022): 1163-1170. doi:10.1016/j.ymthe.2021.09.022

Background

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Pentostatin (2'-deoxycoformycin, Nipent) is an adenosine deaminase inhibitor with a K_i value of 1.2pM and an IC_{50} value of 1.4pM^[1]. Pentostatin is used for hairy cell leukemia treatment, as well as another type of cancer^[2]. The natural adenosine analog is produced by the bacterium *Streptomyces antibioticus* and the fungus *Emmericella nidulans*^[3].

In vitro, Pentostatin (100μM-1nM; 4h) inhibits the growth in soft agar of T cell colonies from PHA-stimulated human peripheral blood lymphocytes^[4]. Pentostatin (1μM) also has the growth-inhibitory activity of 9-beta-D-arabinofuranosyladenine in human cultured cell lines derived from leukemias and lymphomas^[5].

In vivo, Pentostatin (10μg; once; i.v) indirectly triggers Toll-like receptor 3 and enhances immune infiltration in tumors in a C57BL/6 nude mice model^[6]. Pentostatin(0.16mg/kg; once per day; 7d; i.p) also shows cytotoxicity to T cells with a decrease in the number of Thy-1-positive cells in both spleen and lymph nodes in BALB/c (H-2d) mice^[7]. The effect of Pentostatin(10-100μg/g; once; s.c) on the thymus was proven to be independent of the adrenal glands by the use of adrenalectomized mice^[8].

References:

- [1] Adamek, Rebecca N et al. "Identification of Adenosine Deaminase Inhibitors by Metal-binding Pharmacophore Screening." *ChemMedChem* vol. 15,22 (2020): 2151-2156.
doi:10.1002/cmdc.202000271
- [2] "Pentostatin." *LiverTox: Clinical and Research Information on Drug-Induced Liver Injury*, National Institute of Diabetes and Digestive and Kidney Diseases, 12 September 2020.
- [3] Agarwal, R P et al. "Tight-binding inhibitors--IV. Inhibition of adenosine deaminases by various inhibitors." *Biochemical pharmacology* vol. 26,5 (1977): 359-67. doi:10.1016/0006-2952(77)90192-7
- [4] Colledge, N R et al. "Action of deoxycoformycin on human T cell colonies in vitro." *Clinical and experimental immunology* vol. 50,1 (1982): 115-22.
- [5] Kuroki, Y et al. "Potentiation of growth-inhibitory activity of 9-beta-D-arabinofuranosyladenine by 2'-deoxycoformycin in human cultured cell lines derived from leukemias and lymphomas." *Japanese journal of cancer research : Gann* vol. 80,5 (1989): 482-9. doi:10.1111/j.1349-7006.1989.tb02340.x
- [6] Tusup, Marina et al. "Epitranscriptomics modifier pentostatin indirectly triggers Toll-like receptor 3 and can enhance immune infiltration in tumors." *Molecular therapy : the journal of the American Society of Gene Therapy* vol. 30,3 (2022): 1163-1170. doi:10.1016/j.ymthe.2021.09.022
- [7] Tedde, A et al. "Animal model for immune dysfunction associated with adenosine deaminase

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[8] Ratech, H et al. “Effects of deoxycoformycin in mice. III. A murine model reproducing multi-system pathology of human adenosine deaminase deficiency.” *The American journal of pathology* vol. 119,1 (1985): 65-72.

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