

Product Data Sheet

Product Name: LY 345899

Cat. No.: GC31357

Chemical Properties

Cas. No. 10538-99-5

SMILES O=C(O)[C@@H](NC(C1=CC=C(N2C(N3C4=C(NC(N)=NC4=O)NCC3C2)=O)C=C1)=O)CCC(O)=O

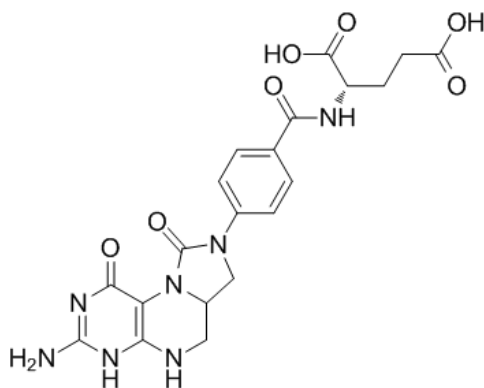
Formula $C_{20}H_{21}N_7O_7$ M.Wt 471.42

Solubility DMSO : 125 mg/mL (265.16 mM) 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]:

Cell lines B cells from the spleens of mice

Caution: Product has not been fully validated for medical applications. For research use only.

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B cells from the spleens of mice were cultivated in a 24-well plate at a density of 5×10^5 cells/ml in RPMI-1640 medium supplemented with 10% fetal calf serum Preparation Method (FCS). Cells were treated daily with either vehicle control (DMSO 0.1% v/v) or 100nM LY 345899. After 2 days of treatment, the cell number and IL-10 levels were determined.

Reaction
Conditions 100nM; 48h

Applications LY 345899 treatment reduced the cell number and IL-10 levels in B cells.

Animal experiment [2]:

Animal models Female BABL/c nude mice

Female BABL/c nude mice (4 weeks old) were maintained in a controlled environment at $22 \pm 3^\circ\text{C}$ and 60% relative humidity under a 12h light/dark cycle, and were given free access to standard rodent nutrition and water. SW620 cells (2×10^6 , in phosphate buffered saline) were subcutaneously injected into the Preparation Method flank of nude mice (5 mice per group). When tumors became palpable, the tumor-bearing mice were randomly assigned to two groups (5 mice per group) by random numbers and treated with LY 345899 (10mg/kg) for 4 weeks (5 times a week; i.p.). Tumor size was measured every 4 days using a caliper, and tumor volume was calculated using the standard formula $V = \text{length} \times \text{width}^2 / 2$.

Dosage form 10mg/kg; 5 times a week for 4 weeks; i.p.

Applications LY 345899 treatment significantly inhibited tumor growth in the SW620 xenograft mouse model.

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References:

- [1] Fu Y, Yu B, Wang Q, et al. Oxidative stress-initiated one-carbon metabolism drives the generation of interleukin-10-producing B cells to resolve pneumonia[J]. Cellular & Molecular Immunology, 2024, 21(1): 19-32.
- [2] Ju H Q, Lu Y X, Chen D L, et al. Modulation of redox homeostasis by inhibition of MTHFD2 in colorectal cancer: mechanisms and therapeutic implications[J]. JNCI: Journal of the National Cancer Institute, 2019, 111(6): 584-596.

Background

LY 345899 is an inhibitor of methylenetetrahydrofolate dehydrogenase (MTHFD) 1 and MTHFD2, with an IC₅₀ value of 96 and 663nM, respectively [1]. LY 345899 can selectively target cancer cells by inhibiting MTHFD2, interfering with purine synthesis and 1-Carbon metabolism, while not damaging healthy normal cells [2]. LY 345899 has been widely used to inhibit the cyclohydrolase activity of MTHFD1 and induce growth defects in K562 cells[3].

In vitro, LY 345899 treatment (100nM) for 48 hours significantly reduced the number of B cells of the mouse spleen and inhibited the expression and secretion levels of IL-10[4]. Treatment with 10μM LY 345899 for 20 minutes significantly increased the infarct area in the isolated hearts of intact wild-type female mice after ischemia/reperfusion[5].

In vivo, LY 345899 treatment via intraperitoneal injection at a dose of 10mg/kg (5 times a week) for 4 weeks significantly inhibited tumor growth in the SW620 xenograft mouse model, without affecting the body weight of the mice[6].

References:

- [1] Gustafsson R, Jemth A S, Gustafsson N M S, et al. Crystal structure of the emerging cancer target MTHFD2 in complex with a substrate-based inhibitor[J]. Cancer research, 2017, 77(4): 937-948.
- [2] Tedeschi P M, Vazquez A, Kerrigan J E, et al. Mitochondrial methylenetetrahydrofolate dehydrogenase (MTHFD2) overexpression is associated with tumor cell proliferation and is a novel target for drug development[J]. Molecular Cancer Research, 2015, 13(10): 1361-1366.
- [3] Flickinger K M, Wilson K M, Rossiter N J, et al. Conditional lethality profiling reveals anticancer

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mechanisms of action and drug-nutrient interactions[J]. Science Advances, 2024, 10(40): eadq3591.

[4] Fu Y, Yu B, Wang Q, et al. Oxidative stress-initiated one-carbon metabolism drives the generation of interleukin-10-producing B cells to resolve pneumonia[J]. Cellular & Molecular Immunology, 2024, 21(1): 19-32.

[5] Garbus-Grant H, Ebenebe-Kasonde O V, Kabir R, et al. Formate reduces ischemic injury in female hearts lacking alcohol dehydrogenase 5[J]. FASEB BioAdvances, 2025, 7(12): e70075.

[6] Ju H Q, Lu Y X, Chen D L, et al. Modulation of redox homeostasis by inhibition of MTHFD2 in colorectal cancer: mechanisms and therapeutic implications[J]. JNCI: Journal of the National Cancer Institute, 2019, 111(6): 584-596.

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