LY 345899

Cat. No.: HY-101943

CAS No.: 10538-99-5

Molecular Formula: $C_{20}H_{21}N_7O_7$

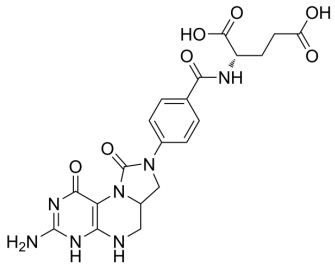
Molecular Weight: 471.42

Target: Methylenetetrahydrofolate Dehydrogenase (MTHFD)

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (265.16 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1213 mL	10.6063 mL	21.2125 mL
	5 mM	0.4243 mL	2.1213 mL	4.2425 mL
	10 mM	0.2121 mL	1.0606 mL	2.1213 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.30 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.41 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.41 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LY 345899 is a Folate analog and is a methylene tetrahydrofolate dehydrogenase (MTHFD1; DC301) and MTHFD2 inbhibitor with IC_{50} values of 96 nM and 663 nM, respectively and a K_i of 18 nM for MTHFD1[1][2][3].

IC_{50} & Target

Ki: 18 nM (MTHFD1)[1]; IC50: 96 nM (MTHFD1) and 663 nM (MTHFD2)[3]

In Vitro

LY 345899 could suppress the MTHFD enzyme in the cytoplasm and mitochondria[4].

	?LY 345899 could disturb the NADPH and redox homeostases and accelerate cell death under oxidative stress, such as hypoxia, or causing in vitro anchorage independence and in vivo impaired tumor growth and metastasis[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	LY345899 (Intraperitoneal injection; 5-10 mg/kg; 5 d/wk; 4 weeks) shows potent antitumor activity and displays therapeutic activity against CRC in vivo[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	SW620 or PDX-based BABL/c nude colorectal cancer (CRC) model[4]
Dosage:	5-10 mg/kg
Administration:	Intraperitoneal injection; 5-10 mg/kg; 5 d/wk; 4 weeks
Result:	Displayed lower cell proliferation indices and higher cell apoptosis. Exhibited no statistically significant weight loss or other signs of acute or delayed toxicity in mice.

CUSTOMER VALIDATION

- Biomed Pharmacother. 2023 Feb 22;161:114412.
- Cancers (Basel). 2021 Jan 23;13(3):425.
- J Biol Chem. 2023 Jun 10;104909.
- bioRxiv. 2021 Feb 3.

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REFERENCES

[1]. Schmidt A, et al. Structures of three inhibitor complexes provide insight into the reaction mechanism of the human methylenetetrahydrofolate dehydrogenase/cyclohydrolase. Biochemistry. 2000 May 30;39(21):6325-35.

[2]. Tedeschi PM, et al. Mitochondrial Methylenetetrahydrofolate Dehydrogenase (MTHFD2) Overexpression Is Associated with Tumor Cell Proliferation and Is a Novel Target for Drug Development. Mol Cancer Res. 2015 Oct;13(10):1361-6.

[3]. Gustafsson R, et al. Crystal Structure of the Emerging Cancer Target MTHFD2 in Complex with a Substrate-Based Inhibitor. Cancer Res. 2017 Feb 15;77(4):937-948.

[4]. Huai-Qiang Ju, et al.Modulation of Redox Homeostasis by Inhibition of MTHFD2 in Colorectal Cancer: Mechanisms and Therapeutic Implications. J Natl Cancer Inst. 2019 Jun 1;111(6):584-596.

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