

Product Data Sheet

Product Name: Ambrisentan

Cat. No.: GC17184

Chemical Properties

Cas. No. 177036-94-1

Chemical Name (2S)-2-(4,6-dimethylpyrimidin-2-yl)oxy-3-methoxy-3,3-diphenylpropanoic acid

SMILES CC1=CC(=NC(=N1)OC(C(=O)O)C(C2=CC=CC=C2)(C3=CC=CC=C3)OC)C

Formula C₂₂H₂₂N₂O₄

M.Wt 378.42

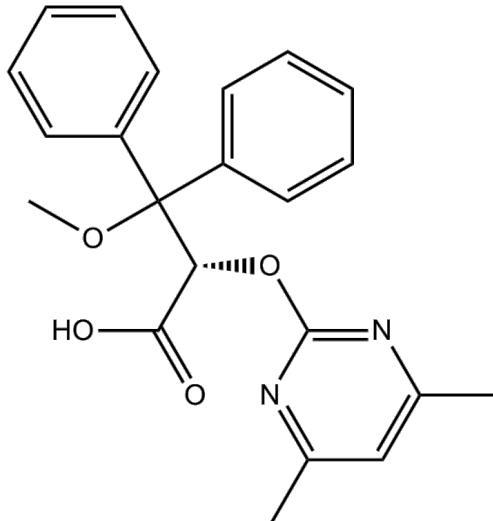
Solubility ≥ 18.921mg/mL in DMSO

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 Human pulmonary artery endothelial cells (hPAECs)

The hPAECs were seeded in 6-well petri dishes at a density of 2×10^5 cells/well. Hypoxia was induced by exposure to a mixture of 4% O₂, 4% CO₂, and 92% N₂ at 37°C for 24 hours. Cells were divided into control glucose concentration

Preparation Method (vehicle, 5.5mM, control and 285mOsm/l), high glucose concentration (HG: 30.5mM and 385mOsm/l), high mannitol concentration (HM: 5.5mM glucose+25mM and 385mOsm/l) for 24h, and were incubated under normoxic or hypoxic conditions with or without Ambrisentan (0.02nM). At the end of the treatment, cells were harvested for autophagy detection.

Reaction Conditions 0.02nM; 24h

Applications Ambrisentan treatment increased autophagy in hPAECs treated with high glucose under hypoxia/normoxia.

Animal experiment [2]:

Animal models BALB/c mice

BALB/c mice were maintained in a standard sterile environment with a controlled 12-h light/dark cycle and ad libitum access to rodent feed and water.

Preparation Method 4T1 cells (2×10^4 cells, volume 100μl) were subcutaneously injected into the fourth mammary fat pad of 8-week-old mice. Mice were randomly divided into two groups. The first group was treated with ddH₂O by gavage daily for 5 days, followed by 2 days of rest for 2 weeks. The second group received Ambrisentan 10mg/kg/day for two weeks after tumor cell implantation. Mice were sacrificed on day 21 after implantation, and liver tissues were removed for analysis.

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Dosage form 10mg/kg/day for 14 days; p.o.

Applications Ambrisentan treatment significantly reduced the liver metastatic foci in 4T1 breast tumor-bearing mice.

References:

- [1] Cabiati M, Biondi F, Ghelardoni S, et al. Ambrisentan Retains Its Pro-Autophagic Activity on Human Pulmonary Artery Endothelial Cells Exposed to Hypoxia in an In Vitro Model Mimicking Diabetes[J]. Journal of Cellular and Molecular Medicine, 2025, 29(7): e70528.
- [2] Kappes L, Amer R L, Sommerlatte S, et al. Ambrisentan, an endothelin receptor type A-selective antagonist, inhibits cancer cell migration, invasion, and metastasis[J]. Scientific reports, 2020, 10(1): 15931.

Background

Ambrisentan is an orally active, highly selective antagonist of endothelin receptor ETA-selective antagonist, with an IC_{50} value of 0.6nM^[1]. Ambrisentan inhibits the OATP1B1 and OATP1B3, with IC_{50} values of 47.0 and 44.6 μ M, respectively^[2]. Ambrisentan has been widely used to improve liver function and hemodynamics in rat models of nonalcoholic steatohepatitis^[3].

In vitro, Ambrisentan treatment at 50 μ M for 4 days significantly increased the mRNA levels of ABCB1 and CYP2C9 in LS180 cells^[4]. Under hypoxic conditions, 0.02nM Ambrisentan treatment for 24h markedly enhanced autophagy in high glucose-treated human pulmonary artery endothelial cells (hPAECs)^[5].

In vivo, Ambrisentan treatment via oral administration at a dose of 10mg/kg/day for 2 weeks significantly inhibited liver metastasis, reduced myeloid cell accumulation, and improved survival in 4T1 breast cancer-bearing mice^[6]. Intraperitoneal injection of Ambrisentan at a dose of 5mg/kg/day for one week significantly reduced portal vein injury and alleviated biliary senescence in Mdr2^{-/-} mice^[7]. Oral administration of Ambrisentan at a dose of 2.5mg/kg/day for 4 weeks attenuated the progression of liver fibrosis without affecting steatosis in a mouse model of nonalcoholic

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steatohepatitis^[8].

References:

- [1] Hou J, Liu S, Zhang X, et al. Structural basis of antagonist selectivity in endothelin receptors[J]. Cell Discovery, 2024, 10(1): 79.
- [2] Lepist E I, Gillies H, Smith W, et al. Evaluation of the endothelin receptor antagonists ambrisentan, bosentan, macitentan, and sitaxsentan as hepatobiliary transporter inhibitors and substrates in sandwich-cultured human hepatocytes[J]. PloS one, 2014, 9(1): e87548.
- [3] Bravo M, Raurell I, Barberá A, et al. Synergic effect of atorvastatin and ambrisentan on sinusoidal and hemodynamic alterations in a rat model of NASH[J]. Disease models & mechanisms, 2021, 14(5): dmm048884.
- [4] Weiss J, Herzog M, Haefeli W E. Differential modulation of the expression of important drug metabolising enzymes and transporters by endothelin-1 receptor antagonists ambrisentan and bosentan in vitro[J]. European journal of pharmacology, 2011, 660(2-3): 298-304.
- [5] Cabiati M, Biondi F, Ghelardoni S, et al. Ambrisentan Retains Its Pro-Autophagic Activity on Human Pulmonary Artery Endothelial Cells Exposed to Hypoxia in an In Vitro Model Mimicking Diabetes[J]. Journal of Cellular and Molecular Medicine, 2025, 29(7): e70528.
- [6] Kappes L, Amer R L, Sommerlatte S, et al. Ambrisentan, an endothelin receptor type A-selective antagonist, inhibits cancer cell migration, invasion, and metastasis[J]. Scientific reports, 2020, 10(1): 15931.
- [7] Owen T, Carpino G, Chen L, et al. Endothelin receptor-A inhibition decreases ductular reaction, liver fibrosis, and angiogenesis in a model of cholangitis[J]. Cellular and Molecular Gastroenterology and Hepatology, 2023, 16(4): 513-540.
- [8] Okamoto T, Koda M, Miyoshi K, et al. Antifibrotic effects of ambrisentan, an endothelin-A receptor antagonist, in a non-alcoholic steatohepatitis mouse model[J]. World Journal of Hepatology, 2016, 8(22): 933.

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