Data Sheet (Cat.No.T10480L)

TargetMol

Bay 41-4109

Chemical Properties

CAS No. : 298708-81-3

Formula: C18H13ClF3N3O2

Molecular Weight: 395.76

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	BAY 41-4109 (Methyl (4R)-4-(2-chloro-4-fluorophenyl)-2-(3,5-difluoropyridin-2-yl)-6-methyl-1,4-dihydropyrimidine-5-carboxylate) is a potent inhibitor of human hepatitis B virus (HBV)(IC50 : 53 nM).
Targets(IC50)	HBV
In vitro	Method: In HepG2.2.15 cells, the inhibitory effects of BAY 41-4109 on HBV DNA release and cytoplasmic HBcAg levels were measured, and the half-maximal inhibitory concentrations (IC50) were calculated. The dose-response relationship for both parameters and the association between the anti-HBV mechanism and HBcAg inhibition were evaluated. Result: The IC50 values of BAY 41-4109 for inhibiting HBV DNA release and cytoplasmic HBcAg levels were 32.6 nM and 132 nM, respectively, indicating a stronger inhibitory effect on HBV DNA. Both HBV DNA and HBcAg were inhibited in a dose-dependent manner, suggesting that the anti-HBV mechanism is associated with and dependent on the rate of HBcAg inhibition [1]. Method: Human HepG2.2.15 cells were treated with BAY 41-4109 for 8 days. Inhibition of HBV DNA was detected using dot-blot hybridization and quantified by LumiImager, and cytotoxicity (CC50) was also determined. Result: The IC50 of BAY 41-4109 for inhibiting HBV replication was approximately 53 nM, and the CC50 in HepG2.2.15 cells was approximately 7 μM [3]. Method: HepAD38 cells were treated with BAY 41-4109 (2 μM) for 6 days. Supernatant HBV DNA was quantified by qPCR, and HBeAg and HBsAg levels were measured by ELISA. Result: Following BAY 41-4109 treatment, HBV DNA inhibition exceeded 95% (residual DNA was 4.9% ± 2.8% of the DMSO control), and HBeAg secretion was significantly reduced (to 31.8% ± 3.8% of the control), with an EC50 of 0.05 ± 0.003 μM [4].
In vivo	Method: In a transgenic mouse model, the effect of BAY 41-4109 treatment on HBV replication was evaluated. Result: BAY 41-4109 inhibited HBV virion production at nanomolar concentrations in an animal model. Its mechanism of action involves targeting the viral capsid protein, leading to the formation of aberrant capsids and subsequently suppressing viral replication [2]. Method: HBV transgenic mice (Tg [HBV1.3 fsX-3'5']) were orally administered BAY 41-4109 (3-30 mg/kg) twice daily (b.i.d.) or three times daily (t.i.d.) for 28 days. Hepatic

In vivo	HBV DNA was detected by dot-blot hybridization, plasma HBV DNA was quantified by real-time qPCR, and HBcAg expression in liver tissues was examined by immunohistochemistry. Result: BAY 41-4109 reduced hepatic and plasma HBV DNA levels in a dose-dependent manner, with significant effects observed at doses of 30 mg/kg and 15 mg/kg ($P < 0.05$). Unlike 3TC, BAY 41-4109 markedly reduced HBcAg in the cytoplasm of hepatocytes, suggesting a mechanism of action distinct from that of nucleoside analogs. Pharmacokinetic analysis revealed an oral bioavailability of 30% in mice and a half-life of approximately 2 hours [3].

Solubility Information

Solubility	DMSO: 80 mg/mL (202.14 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 3.3 mg/mL (8.34 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5268 mL	12.6339 mL	25.2678 mL
5 mM	0.5054 mL	2.5268 mL	5.0536 mL
10 mM	0.2527 mL	1.2634 mL	2.5268 mL
50 mM	0.0505 mL	0.2527 mL	0.5054 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Wu GY, et al. Inhibition of hepatitis B virus replication by Bay 41-4109 and its association with nucleocapsid disassembly. J Chemother. 2008;20(4):458-467.
Yang Y, Yan Y, Yin J, et al. Structure-Based Discovery of N-Sulfonylpiperidine-3-carboxamides as Novel Capsid Assembly Modulators for Potent Inhibition of HBV Replication. Viruses. 2022, 14(2): 348.
Yin J, Feng Z, Li Z, et al.Synthesis and evaluation of N-sulfonylpiperidine-3-carboxamide derivatives as capsid assembly modulators inhibiting HBV in vitro and in HBV-transgenic mice.European Journal of Medicinal Chemistry. 2023: 115141.
Stray SJ, et al. BAY 41-4109 has multiple effects on Hepatitis B virus capsid assembly. J Mol Recognit. 2006;19(6): 542-548.
Weber O, et al. Inhibition of human hepatitis B virus (HBV) by a novel non-nucleosidic compound in a transgenic mouse model. Antiviral Res. 2002 May;54(2):69-78.
Yin J, et al.Synthesis and evaluation of N-sulfonylpiperidine-3-carboxamide derivatives as capsid assembly modulators inhibiting HBV in vitro and in HBV-transgenic mice.European Journal of Medicinal Chemistry.2023: 115141.