Ledipasvir D-tartrate

Cat. No.: HY-15602B

CAS No.: 1502654-87-6

Molecular Formula: $C_{53}H_{60}F_2N_8O_{12}$

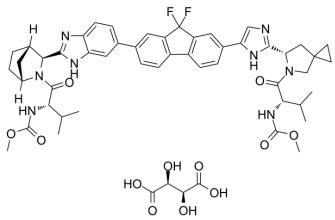
Molecular Weight: 1039.09

Target: HCV

Pathway: Anti-infection

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (24.06 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	0.9624 mL	4.8119 mL	9.6238 mL
	5 mM	0.1925 mL	0.9624 mL	1.9248 mL
	10 mM	0.0962 mL	0.4812 mL	0.9624 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (2.41 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (2.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ledipasvir D-tartrate is an inhibitor of the hepatitis C virus NS5A, with EC_{50} values of 34 pM against GT1a and 4 pM against GT1b replicon.

IC_{50} & Target

EC50: 34 pM (GT1a), 4 pM (GT1b)[1]

In Vitro

Ledipasvir has GT1a and 1b EC_{50} values of 31 and 4 pM, respectively, and protein-adjusted EC_{50} values of 210 pM (GT1a) and 27 pM (GT1b) and the intrinsic EC_{50} of 39 is 310 fM for GT1a and 40 fM for GT1b. Ledipasvir is highly protein-bound both in human serum and in the cell-culture medium (containing 10% BSA) of the replicon assay[1]. Ledipasvir exhibits an EC_{50} value of 141 nM against the JFH/3a-NS5A replicon[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	Ledipasvir is remarkable not only on the basis of its high replicon potency but also on the basis of its low clearance, good bioavailability, and long half-lives in rat, dog, and monkey and low predicted clearance in human. The pharmacokinetics of Ledipasvir is measured in rats and dogs. Ledipasvir shows good half-lives (rat 1.83 ± 0.22 hr, dog 2.63 ± 0.18 hr) in plasma, low systemic clearance (CL), and moderate volumes of distribution (Vss) that are greater than total body water volume[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats, Dogs and Monkeys[1] Pharmacokinetic studies are performed in male naïve Sprague-Dawley(SD) rats, non-naïve beagle dogs, and cynomolgus monkeys (three animals per dosing route). Intravenous (IV) administration is dosed via infusion over 30 min in a vehicle containing 5% ethanol, 20% PEG400, and 75% water (pH adjusted to 3.0 with HCl). Oral dosing is administered by gavage in a vehicle containing 5% ethanol, 45% PEG 400, and 50% of 50 mM citrate buffer, pH 3. Blood samples are collected over a 24 h period postdose into Vacutainer tubes containing EDTA-K2. Plasma was isolated, and the concentration of the test compound in plasma was determined with LC/MS/MS after protein precipitation with acetonitrile. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2021 May 29;6(1):212.
- Proc Natl Acad Sci U S A. 2017 Feb 21;114(8):1922-1927.
- J Gastroenterol. 2019 May;54(5):449-458.
- Int J Radiat Oncol Biol Phys. 2016 Nov 15;96(4):867-876.
- Antimicrob Agents Chemother. 2015 Jun;59(6):3482-92.

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REFERENCES

[1]. Link JO, et al. Discovery of ledipasvir (GS-5885): a potent, once-daily oral NS5A inhibitor for the treatment of hepatitis C virus infection. J Med Chem. 2014 Mar 13;57(5):2033-46

[2]. Hernandez D, et al. Natural prevalence of NS5A polymorphisms in subjects infected with hepatitis C virus genotype 3 and their effects on the antiviral activity of NS5A inhibitors. J Clin Virol. 2013 May;57(1):13-8.

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

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