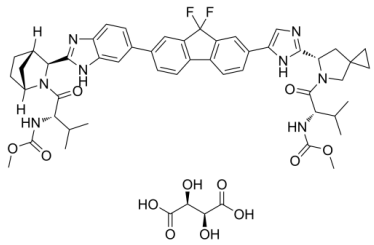
Data Sheet

Product Name:	Ledipasvir (D-tartrate)
Cat. No.:	CS-1980
CAS No.:	1502654-87-6
Molecular Formula:	$C_{53}H_{60}F_2N_8O_{12}$
Molecular Weight:	1039.09
Target:	HCV
Pathway:	Anti-infection
Solubility:	DMSO : 25 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

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. IC50 & 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]. ***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].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: 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) [1].

Oral dosing is administered by gavage in a vehicle containing 5% ethanol, 45% PEG 400, and 50% of 50 mM citrate buffer, pH 3 [1].

[1]Rat, Dog and Monkey[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.

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.

CAIndexNames:

Carbamic acid, N-[(1S)-1-[[(6S)-6-[5-[9,9-difluoro-7-[2-[(1R,3S,4S)-2-[(2S)-2-[(methoxycarbonyl)amino]-3-methyl-1-oxobutyl]-2-azabicyclo[2.2.1]hept-3-yl]-1H-benzimidazol-6-yl]-9H-fluoren-2-yl]-1H-imidazol-2-yl]-5-azaspiro[2.4]hept-5-yl]carbonyl]-2-methylpropyl]-, methyl ester, (2S,3S)-2,3-dihydroxybutanedioate (1:x)

SMILES:

O=C(OC)N[C@H](C(N([C@H](C1=NC=C(C2=CC(C(F)(F)C3=C4C=CC(C5=CC=C6N=C([C@H]7N(C([C@@H](NC(OC)=O)C(C)C)=O)[C@]8([H])CC[C@@]7([H])C8)NC6=C5)=C3)=C4C=C2)N1)C9)CC%109CC%10)=O)C(C)C.O[C@@H]([C@@H](C(O)=O)O)C(O)=O

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

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