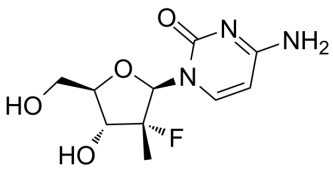
PSI-6130

Cat. No.:	HY-10165
CAS No.:	817204-33-4
Molecular Formula:	$C_{10}H_{14}FN_3O_4$
Molecular Weight:	259.23
Target:	HCV
Pathway:	Anti-infection
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (96.44 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.8576 mL	19.2879 mL	38.5758 mL
5 mM	0.7715 mL	3.8576 mL	7.7152 mL
10 mM	0.3858 mL	1.9288 mL	3.8576 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 (9.64 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (9.64 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (9.64 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PSI-6130 is a potent and selective inhibitor of HCV NS5B polymerase, and inhibits HCV replication with a mean IC_{50} of 0.6 μM.

IC_{50} & Target

IC50: 0.6 μM (HCV replication)[2]

In Vitro

PSI-6130 exhibits potent and specific inhibitory activity against HCV RNA replication mediated by the NS5B polymerase. Both PSI-6130 inhibit HCV GT-1b (Con1 strain) and GT-1a (H77 strain) subgenomic RNA replication, with mean EC_{50} values of

0.51 and 0.30 μM, respectively. PSI-6130 inhibits 40% human serum with EC_{50} of 0.51 μM[1]. PSI-6130 inhibits HCV replication with a mean IC_{50} of 0.6 μM, PSI-6130-TP inhibits HCV replicase with a mean IC_{50} of 0.34 μM. PSI-6130-TP inhibits recombinant HCV Con1 NS5B on a heteropolymeric RNA template derived from the 3′-end of the negative strand of the HCV genome with an IC_{50} of 0.13 μM and K_i of 0.023 μM[2].

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

PROTOCOL

Kinase Assay [1]

The inhibition potency of compounds with respect to the RdRp activity of recombinant NS5B570-BK, NS5B570-Con1, and NS5B570-H77 proteins is determined by measuring the incorporation of radiolabeled NMP into acid-insoluble RNA products by use of a complement strand of internal ribosomal entry site (cIRES) RNA template. Briefly, 50% inhibitory concentration (IC_{50}) determinations are carried out using 200 nM in vitro-transcribed cIRES RNA template, 1 μCi of tritiated UTP (42 Ci/mmol), 500 μM ATP, 500 μM GTP, 1 μM CTP, 1× TMDN buffer (40 mM Tris-HCl [pH 8.0], 4 mM $MgCl_2$, 4 mM dithiothreitol, 40 mM NaCl), and 200 nM enzyme. The inhibition potency of compounds with respect to the RdRp activity of NS5B570-S282T-Con1 is determined under GT-1b assay conditions as. NS5B570-BK and NS5B570-Con1 enzymes are used as controls. The final reaction volume is 50 μL under all assay conditions. All reactions contain a final 10% dimethyl sulfoxide. K_m and K_i values are measured.

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

CUSTOMER VALIDATION

- Antiviral Res. 2019 Oct;170:104570.

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REFERENCES

[1]. Ali S, et al. Selected replicon variants with low-level in vitro resistance to the hepatitis C virus NS5B polymerase inhibitor PSI-6130 lack cross-resistance with R1479. Antimicrob Agents Chemother. 2008 Dec;52(12):4356-69.

[2]. Ma H, et al. Characterization of the metabolic activation of hepatitis C virus nucleoside inhibitor beta-D-2'-Deoxy-2'-fluoro-2'-C-methylcytidine (PSI-6130) and identification of a novel active 5'-triphosphate species. J Biol Chem. 2007 Oct 12;282(41):298

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