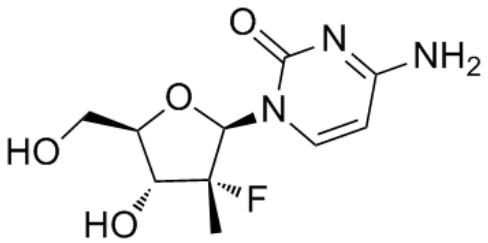
Product Data Sheet

Product Name: PSI-6130
Cat. No.: GC37028

Chemical Properties

Cas. No.	817204-33-4		
SMILES	O=C1N=C(C=CN1[C@@H]([C@@](C)([C@@H]2O)F)O[C@@H]2CO)N		
Formula	$C_{10}H_{14}FN_3O_4$	M.Wt	259.23
Solubility	DMSO: ≥ 50 mg/mL (192.88 mM)	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

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Kinase experiment: 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 (IC50) 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 MgCl2, 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. Km and Ki values are measured.

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):29812-20. Epub 2007 Aug 13.

Background

PSI-6130 is a potent and selective inhibitor of HCV NS5B polymerase, and inhibits HCV replication with a mean IC50 of 0.6 μM. IC50: 0.6 μM (HCV replication)[2]

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 EC50 values of 0.51 and 0.30 μM, respectively. PSI-6130 inhibits 40% human serum with EC50 of 0.51 μM[1]. PSI-6130 inhibits HCV replication with a mean

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IC50 of 0.6 μM, PSI-6130-TP inhibits HCV replicase with a mean IC50 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 IC50 of 0.13 μM and Ki of 0.023 μM[2].

[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):29812-20. Epub 2007 Aug 13.

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