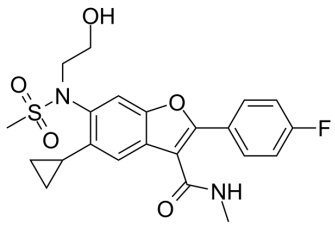
Nesbuvir

Cat. No.:	HY-14775
CAS No.:	691852-58-1
Molecular Formula:	$C_{22}H_{23}FN_2O_5S$
Molecular Weight:	446.49
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 : ≥ 50 mg/mL (111.98 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2397 mL	11.1985 mL	22.3969 mL
	5 mM	0.4479 mL	2.2397 mL	4.4794 mL
	10 mM	0.2240 mL	1.1198 mL	2.2397 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 (5.60 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.60 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.60 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Nesbuvir is a nonnucleoside inhibitor of the hepatitis C virus (HCV) nonstructural protein 5B (NS5B) polymerase.
IC_{50} & Target	EC50: 9 nM ($NS3^{V170A}$), 13 nM ($NS3^{V170A}$), 15 nM ($NS3^{K583T}$), 13 nM ($NS5B^{I424V}$)[1]
In Vitro	Replicon cells are treated with 1 mg/mL G418 and combinations of the two compounds. Nesbuvir (HCV-796) is added to 40 or 80 nM (approximately 10 and 20 times the EC_{50} in a 3-day replicon inhibition assay, respectively) and Boceprevir is added

	to 400 or 800 nM (approximately 2 and 4 times the EC_{50}, respectively). The EC_{50}s for Nesbuvir and Boceprevir for the parental replicon in the transient expression assay are comparable to those obtained in the 3-day inhibition assay with the stable replicon cells; the EC_{50} for Nesbuvir in the transient expression assay is 14 nM, whereas it is 5 nM for the stable replicon; and the EC_{50} for Boceprevir in the transient expression assay is 608 nM, whereas it is 201 nM for the stable replicon[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Among a huge variety of yet characterized nucleoside and non-nucleoside inhibitors (NNI), the benzofurane derivative NNI Nesbuvir (HCV-796) is demonstrated to yield significant antiviral effects in mice with chimeric human livers and in patients infected with HCV. HCV-796 binds to a hydrophobic binding pocket at the “palm” domain of NS5B; however, its mode of inhibition remains to be defined[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Huh7-BB7 cells are seeded at a density of 20,000 cells per 100 mm dish in DMEM supplemented with 2% FBS, 1 mg/mL G418, and various concentrations of Nesbuvir and/or Boceprevir with DMSO at a final concentration of 0.5% (vol/vol). The medium is removed and is replaced with fresh medium with the appropriate compound concentrations every 3 or 4 days. After 7 days, the cells are split 1 to 10, placed into fresh 100 mm dishes, and incubated with medium with the appropriate compound concentrations. After 20 days, the medium is removed and the cells are fixed with 7% (wt/vol) formaldehyde and stained with 1% (wt/vol) crystal violet in 50% (vol/vol) ethanol[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2017 Feb 21;114(8):1922-1927.
- Antiviral Res. 2017 Oct;146:65-75.
- Antiviral Res. 2017 Mar;139:18-24.
- Antimicrob Agents Chemother. 2019 May 24;63(6). pii: e00003-19.
- Antimicrob Agents Chemother. 2014 Dec;58(12):7215-24.

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REFERENCES

[1]. Flint M, et al. Selection and characterization of hepatitis C virus replicons dually resistant to the polymerase and protease inhibitors HCV-796 and boceprevir (SCH 503034). Antimicrob Agents Chemother. 2009 Feb;53(2):401-11.

[2]. Reich S, et al. Mechanisms of activity and inhibition of the hepatitis C virus RNA-dependent RNA polymerase. J Biol Chem. 2010 Apr 30;285(18):13685-93.

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