Product Data Sheet

Product Name: Daclatasvir (BMS-790052)
Cat. No.: GC12057

Chemical Properties

Cas. No.	1214735-16-6		
Chemical Name	methyl N-[(2S)-1-[(2S)-2-[5-[4-[4-[2-[(2S)-1-[(2S)-2-(methoxycarbonylamino)-3-methylbutanoyl]pyrrolidin-2-yl]-1H-imidazol-5-yl]phenyl]phenyl]-1H-imidazol-2-yl]pyrrolidin-1-yl]-3-methyl-1-oxobutan-2-yl]carbamate		
SMILES	CC(C)C(C(=O)N1CCCC1C2=NC=C(N2)C3=CC=C(C=C3)C4=CC=C(C=C4)C5=CN=C(N5)C6CCCN6C(=O)C(C(C)C)NC(=O)OC)NC(=O)C		
Formula	$C_{40}H_{50}N_8O_6$	M.Wt	738.88
Solubility	≥ 36.6mg/mL in DMSO, ≥ 23.33 mg/mL in EtOH with ultrasonic	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	Daclatasvir (BMS-790052)		

Protocol

Cell experiment [1]:

Cell lines	HCV genotypes and the JFH-1 genotype 2a infectious virus in cell culture
Preparation method	The solubility of this compound in DMSO is > 36.6 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 ℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting condition	EC50: 9 to 146 pM
Applications	BMS-790052 exhibited picomolar half-maximum effective concentrations towards replicons expressing a broad range of HCV genotypes and the JFH-1 genotype 2a infectious virus in cell culture, with EC50 values ranging from 9 to 146 pM. BMS-790052 displayed similar potency in Huh-7, HeLa and HEK293T cells.

Animal experiment [1]:

Animal models	patients chronically infected with HCV
Dosage form	Oral administration, 10-100 mg
Application	BMS-790052 was safe and well tolerated in HCV-infected subjects after single oral doses up to 100 mg. In HCV-infected subjects, BMS-790052 had a mean plasma elimination half-life ranging from 10 to 14 h. Administration of a single 100-mg dose of BMS-790052 was associated with a 3.3log 10 reduction in mean viral load measured 24h post-dose that was sustained for an additional 120h in two patients infected with genotype 1b virus.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Gao M, Nettles R E, Belema M, et al. Chemical genetics strategy identifies an HCV NS5A inhibitor with a potent clinical effect[J]. Nature, 2010, 465(7294): 96.

Background

Daclatasvir, formerly known as BMS-790052, is a potent NS5A inhibitor with EC50 values varying from 9 to 146 pM. [1,2]
The nonstructural 5A (NS5A) is a target in HCV drug development, which is a 447 amino-acid, zinc-binding phosphoprotein who plays an essential but enigmatic role in the virus life cycle. However the function of NS5A has no enzymatic activities, which makes it very difficult to understand the antiviral function of daclatasvir. It is assumed that Daclatasvir may interfere with the dimeric structure of NS5A, effecting subtle structural distortions that interfere with protein function in a specific way.[1,2]
The antiviral activity of daclatasvir towards genotypes was assessed by using replication-competent 1a or 1b replicons to construct hybrids in which the entire NS5A coding region or the first 100 amino acids of NS5A from different genotypes replaced the corresponding sequence of the parent replicon. Daclatasvir was reported to be highly potent across all HCV genotypes with half-maximum effective concentrations (EC50) ranging from 9 to 146 pM.[2]
A phase I clinical study showed Daclatasvir's inhibition for HCV viruses. A 1 mg dose of daclatasvir produced a mean 1.8 log10 reduction in serum HCV RNA 24 h after administration. The 10 and 100 mg doses produced 3.2 log10 and 3.3 log10 reductions, respectively. Data collected from clinical trials on daclatasvir illustrated an initial, rapid viral decline followed by a slower fall in HCV RNA, which indicated that by inhibiting NS5A, daclatasvir blocks intracellular HCV RNA synthesis and virion assembly and secretion.[1]
References:
1.Herbst D A, Reddy K R. NS5A inhibitor, daclatasvir, for the treatment of chronic hepatitis C virus infection[J]. Expert opinion on investigational drugs, 2013, 22(10): 1337-1346.
2.Gao M, Nettles R E, Belema M, et al. Chemical genetics strategy identifies an HCV NS5A inhibitor with a potent clinical effect[J]. Nature, 2010, 465(7294): 96-100.

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