Daclatasvir (BMS-790052)

Catalog No.C07833 Batch:C0783303

Product Datasheet

Technical Data

Formula	$C_{40}H_{50}N_8O_6$					
Molecular Weight	738.88	**CAS No.**	1009119-64-5			
Solubility (25°C)*	In vitro	DMSO	148 mg/mL (200.3 mM)			
		Ethanol	148 mg/mL (200.3 mM)			
		Water	Insoluble			
	In vivo (Add solvents to the product individually and in order)	Oral Administration	Homogeneous suspension	CMC-NA	≥5mg/ml	Taking the 1 mL working solution as an example, add 5 mg of this product to 1 ml of CMC-Na solution, mix evenly to obtain a homogeneous suspension with a final concentration of 5 mg/ml.

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Capsid Bio tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.
* Room temperature shipping (Stability testing shows this product can be shipped at 2-8°C for storage purposes.)

Preparing Stock Solutions

Concentration \ Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.3534 mL	6.7670 mL	13.5340 mL
5 mM	0.2707 mL	1.3534 mL	2.7068 mL
10 mM	0.1353 mL	0.6767 mL	1.3534 mL
50 mM	0.0271 mL	0.1353 mL	0.2707 mL

Biological Activity

Description	Daclatasvir (BMS-790052, EBP883) is a highly selective inhibitor of **HCV NS5A** with **EC50** of 9-50 pM, for a broad range of HCV replicon genotypes and the JFH-1 genotype 2a infectious virus in cell culture. Phase 3.
Targets	HCV NS5A [1] 9 pM-50 pM(EC50)
In vitro	Daclatasvir (BMS-790052) is one of the most potent inhibitors of HCV replication reported so far. The mean EC50 values of this compound are 50 and 9 pM for HCV genotype 1a and 1b replicons, respectively. It displays a therapeutic index (CC50/EC50) of at least 10^5 and is inactive towards a panel of 10 RNA and DNA viruses, with EC50 higher than 10 μM. This confirms its specificity for HCV. [1] In Huh7 cells harboring the HCV genotype 1b replicons, it blocks both transient and stable HCV genome replication, with EC50 values ranging from 1-15 pM. At concentrations of 100 pM or 1 nM, it has been shown to alter the subcellular localization and biochemical fractionation of NS5A. [2] This compound inhibits hybrid replicons containing HCV genotype-4 NS5A genes with EC50 of 7-13 pM. Residue 30 of NS5A is an important site for BMS-790052-mediated resistance in the hybrid replicons. [3]
Features	First-in-class, highly selective inhibitor of hepatitis C virus (HCV) NS5A with picomolar EC50 values.

Protocol (from reference)

Kinase Assay:[4]

- **FRET assay for HCV NS5A inhibitors**

  该肽（Ac-Asp-Glu-Asp [EDANS]-Glu-Glu-Abu-[COO] Ala-Ser-Lys [DABCYL]-NH2）在其一端附近含有荧光供体{EDANS，5-[(2-氨基乙基）氨基]萘-1-磺酸}，另一端附近含有受体{DABCYL，4-[(4-二甲基氨基）苯基]偶氮}苯甲酸}。供体与受体之间的分子间共振能量转移会淬灭该肽的荧光，但随着NS3蛋白酶切割该肽，产物从共振能量转移淬灭中释放出来。随着更多底物被NS3蛋白酶切割，供体的荧光随时间增强。检测试剂为：5×荧光素酶细胞培养裂解试剂用dH_2O稀释至1×，加入NaCl（150 mM）和FRET肽（20 μM）。将HCV-Huh-7细胞置于96孔板中，并使其附着过夜（每孔$1×10^4$个细胞）。第二天，向孔中加入Daclatasvir (BMS-790052)，并将板孵育72小时。然后用PBS冲洗板，并通过每孔加入30 μL上述FRET肽检测试剂进行FRET检测。使用Cytofluor 4000仪器获取信号，该仪器设置为340 nm（激发）/490 nm（发射）自动模式，运行20个循环或更少，并在动力学模式下读取板。FRET检测后，向每孔加入40 μL荧光素酶底物，并测量荧光素酶活性。

Cell Assay:[1]

- **Cell lines**

  HCV replicon cells (Huh7)

- **Concentrations**

  0.1 pM - 50 μM, dissolved in DMSO (the final concentration of DMSO is 0.5%)

- **Incubation Time**

  72 hours

- **Method**

  Daclatasvir (BMS-790052) is added to 96-well plates containing HCV replicon cells seeded approximately 12 hours before in 200 μL media. The cell plates are tested for replication activity and cytotoxicity after 72 hours of incubation. Cytotoxicity is measured with CellTiter-Blue, after which the media and dye are removed, plates are inverted and the remaining liquid is blotted with paper towels. Replication activity of the HCV genotype 1a cell lines is quantified using Renilla luciferase. 1× Renilla luciferase lysis buffer (30 μL) is added to each well and plates are incubated with gentle shaking for 15 min. Renilla luciferase substrate (40 μL) is then added and the signals are detected using a Top Count luminometer set for light emission quantification. One hundred per cent activity is calculated for each cell line for the DMSO-only wells; percentage activity is calculated for each concentration of the inhibitor by dividing the average value for wells containing this compound by the average value for wells containing DMSO.

References

https://pubmed.ncbi.nlm.nih.gov/20410884/ https://pubmed.ncbi.nlm.nih.gov/21513964/ https://pubmed.ncbi.nlm.nih.gov/22203595/

+ Expand

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