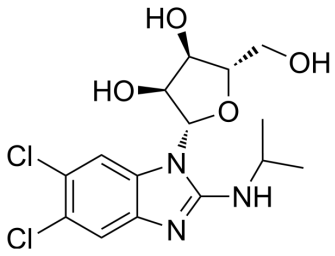
Maribavir

Cat. No.:	HY-16305
CAS No.:	176161-24-3
Molecular Formula:	$C_{15}H_{19}Cl_2N_3O_4$
Molecular Weight:	376.24
Target:	CMV; EBV
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 : 200 mg/mL (531.58 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6579 mL	13.2894 mL	26.5788 mL
	5 mM	0.5316 mL	2.6579 mL	5.3158 mL
	10 mM	0.2658 mL	1.3289 mL	2.6579 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.87 mg/mL (7.63 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.87 mg/mL (7.63 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.64 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.64 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.64 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Maribavir is a potent inhibitor of histone phosphorylation catalyzed by wild-type pUL97 in vitro, with an IC_{50} of 3 nM. Maribavir has potent antiviral activity against HCMV and Epstein-Barr virus (EBV).

IC_{50} & Target	HCMV[1]
In Vitro	Maribavir is a potent inhibitor of the autophosporylation of the wild type and all the major Ganciclovir (GCV) resistant UL97 mutants analysed with a mean IC_{50} of 35 nM. The M460I mutation results in hypersensitivity to Maribavir with an IC_{50} of 4.8 nM. A Maribavir resistant mutant of UL97 (L397R) is functionally compromised as both a Ganciclovir kinase and a protein kinase (~ 10% of wild type levels). Enzyme kinetic experiments demonstrate that Maribavir is a competitive inhibitor of ATP with a K_i of 10 nM[1]. Maribavir (1263W94) inhibits viral replication in a dose-dependent manner, with IC_{50} of 0.12±0.01 μM as measured by a multicycle DNA hybridization assay. The pUL97 protein kinase is strongly inhibited by Maribavir, with 50% inhibition occurring at 3 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Enzyme kinetic analysis is performed on the purified wild type and mutant UL97 protein species using increasing concentrations of ATP (2 μM to 20 μM). The amount of incorporated radiolabelled phosphate is plotted against the concentration of ATP in a Lineweaver Burke plot to determine the K_m for ATP for each UL97 species. The effect of Maribavir upon the rate of radiolabelled phosphate incorporation by wild type or mutant UL97 is determined by protein kinase assays at a fixed concentration of Maribavir (0.5 μM) as above, or with increasing concentrations of Maribavir (0.01 μM to 5.0 μM) to determine the IC_{50} of Maribavir for each UL97 species. In order to determine the nature of the inhibition mediated by Maribavir, plots of 1/v vs 1/ATP with increasing concentrations of Maribavir are constructed. Competitive inhibition is evident if the family of lines cconverged on the y-axis at 1/Vmax. The change in slope caused by the addition of Maribavir is used to calculate the K_i[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	For these studies MRC-5 cells are seeded in 24-well plates at ~5×10^4 cells/well and grown for 3 days in MEM 8-1-1 to confluence (~1.1×10^5 cells/well). The cells are infected with AD169 in MEM 2-1-1 at an MOI ranging from 1 to 3 and incubated at 37°C for 90 min to allow viral adsorption. The unadsorbed virus is removed and replaced with 1 mL of MEM 2-1-1. To test the effect of compounds on viral DNA synthesis or maturation, Maribavir, BDCRB, or GCV is added to the medium at the concentrations indicated for each experiment[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Antiviral Res. 2023 Dec 30:105792.
- Cells. 2023 Apr 14, 12(8), 1162.
- Int J Mol Sci. 2023 Dec 13, 24(24), 17421.
- Int J Mol Sci. 2022 Feb 24;23(5):2493.
- Int J Mol Sci. 2021 Jan 8;22(2):E575.

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REFERENCES

[1]. Shannon-Lowe CD, et al. The effects of Maribavir on the autophosphorylation of ganciclovir resistant mutants of the cytomegalovirus UL97 protein. Herpesviridae. 2010 Dec 7;1(1):4.

[2]. Biron KK, et al. Potent and selective inhibition of human cytomegalovirus replication by 1263W94, a benzimidazole L-riboside with a unique mode of action. Antimicrob

Agents Chemother. 2002 Aug;46(8):2365-72.

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