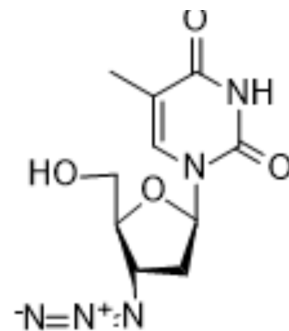


Zidovudine

Cat. No.:	HY-17413		
CAS No.:	30516-87-1		
Molecular Formula:	C ₁₀ H ₁₃ N ₅ O ₄		
Molecular Weight:	267.24		
Target:	HIV; CRISPR/Cas9		
Pathway:	Anti-infection; Cell Cycle/DNA Damage		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (374.20 mM)
 H₂O : 16.67 mg/mL (62.38 mM; ultrasonic and warming and heat to 60°C)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	3.7420 mL	18.7098 mL	37.4195 mL
	5 mM	0.7484 mL	3.7420 mL	7.4839 mL
	10 mM	0.3742 mL	1.8710 mL	3.7420 mL

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

In Vivo

- Add each solvent one by one: PBS
Solubility: 20 mg/mL (74.84 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (9.35 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (9.35 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (9.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zidovudine is a nucleoside reverse transcriptase inhibitor (NRTI), widely used to treat HIV infection. Zidovudine increases CRISPR/Cas9-mediated editing frequency.

IC ₅₀ & Target	HIV-1	CRISPR/Cas9
In Vitro	<p>Zidovudine inhibits SVG, Primary human fetal astrocytes (PFA), peripheral blood mononuclear cells (PBMC), and monocyte-derived macrophages (MDM) with EC₅₀ of 17, 1311, 8, and 5 nM, respectively. Zidovudine inhibits SVG, PFA, PBMC, and MDM with EC₉₀ of 0.205 μM, 44.157 μM, 0.481 μM, and 0.219 μM, respectively^[1]. Genome editing via CRISPR/Cas9 has become an efficient and reliable way to make precise, targeted changes to the genome of living cells. CXCR4 is a co-receptor for the human immunodeficiency virus type 1 (HIV-1) infection and has been considered as an important therapeutic target for AIDS. CXCR4 mediates viral entry into human CD4⁺ cells by binding to envelope protein, gp120. Human CXCR4 gene is efficiently disrupted by CRISPR/Cas9-mediated genome editing, leading to HIV-1 resistance of human primary CD4⁺ T cells. The Cas9-mediated ablation of CXCR4 demonstrated high specificity and negligible off-target effects without affecting cell division and propagation^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>	
In Vivo	<p>Intravitrous injection of the NRTIs Lamivudine (3TC), Zidovudine (AZT), or Abacavir (ABC) suppresses the laser-induced choroidal neovascularization (CNV) in wild-type mice compared to PBS vehicle. The mean level of VEGF-A in the RPE/choroid, which peaks on day 3 after laser injury, is significantly reduced in 3TC-, AZT- and ABC-treated eyes compared with control eyes in wild-type mice, but not in P2rx7^{-/-} mice^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>	

PROTOCOL

Cell Assay ^[1]	<p>Assays are performed in all cell types in the presence of titrating concentrations of ARV. 5,000 SVG, 2,500 PFA, 200,000 PBMC, or 50,000 MDM cells/well are seeded into triplicate wells of 96-well plates. Twenty-four hours later, the culture medium is removed and replaced with medium containing the ARV or DMSO (0.5% vol/vol), and equivalent TCID₅₀ infectious units of luciferase reporter virus are added to the cells. After a 16 h incubation at 37°C, the initial viral inoculum is removed and replaced with culture medium containing the same antiretroviral drug (ARV) or DMSO (0.5% vol/vol) concentrations. At 72 h post infection, the medium is aspirated, the cells are lysed and HIV-1 infection measured using the Luciferase Assay System. Luminescence is measured using a FLUOStar Optima microplate reader. Inhibition curves and the 50% (EC₅₀) and 90% (EC₉₀) effective concentrations are determined by nonlinear regression analysis, using GraphPad Prism software^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Administration ^[3]	<p>Mice^[3]</p> <p>C57BL/6J (wild-type) and P2rx7^{-/-} mice are used. The Nlrp3^{-/-} mice are used. The NRTIs 3TC, AZT, and ABC or the P2X7 antagonist A438079 hydrochloride are dissolved in PBS. For CNV, each group of mice is injected once with 1 μL of NRTIs (3TC, 125 ng/μL; ABC, 183 ng/μL; AZT, 146 ng/μL), 1 μL of A438079 hydrochloride (3, 30, or 300 ng/μL), or the same volume of vehicle (PBS) into the vitreous humor using a 33-gauge needle immediately after laser injury. Another group of mice is injected with 3TC (125 ng) in combination with an anti-mouse VEGF polyclonal antibody (10 ng). Goat whole IgG (10 ng) is used as a biological control for the anti-mouse VEGF antibody.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

CUSTOMER VALIDATION

- Arch Toxicol. 2022 May 17;1-20.
- Int J Antimicrob Agents. 2019 Dec;54(6):814-819.
- Pharmaceutics. 2022, 14(6), 1188.
- Heliyon. 2020 Jun 3;6(6):e04050.
- bioRxiv. 2020 May.

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REFERENCES

- [1]. Gray LR, et al. The NRTIs lamivudine, stavudine and zidovudine have reduced HIV-1 inhibitory activity in astrocytes. PLoS One. 2013 Apr 16;8(4):e62196.
- [2]. Hou P, et al. Genome editing of CXCR4 by CRISPR/cas9 confers cells resistant to HIV-1 infection. Sci Rep. 2015 Oct 20;5:15577.
- [3]. Mizutani T, et al. Nucleoside Reverse Transcriptase Inhibitors Suppress Laser-Induced Choroidal Neovascularization in Mice. Invest Ophthalmol Vis Sci. 2015 Nov;56(12):7122-9.
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