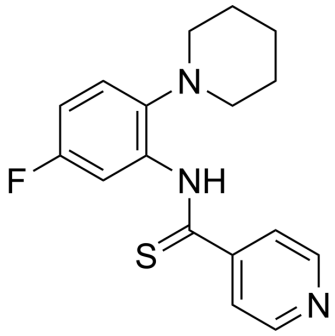
FIT-039



Cat. No.:	HY-18944
CAS No.:	1113044-49-7
Molecular Formula:	$C_{17}H_{18}FN_3S$
Molecular Weight:	315.41
Target:	CDK; HSV; CMV; DNA/RNA Synthesis
Pathway:	Cell Cycle/DNA Damage; Anti-infection
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month

SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (317.05 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1705 mL	15.8524 mL	31.7048 mL
	5 mM	0.6341 mL	3.1705 mL	6.3410 mL
	10 mM	0.3170 mL	1.5852 mL	3.1705 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 (7.93 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (7.93 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.93 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

FIT-039 is a selective, ATP-competitive and orally active CDK9 inhibitor with an IC_{50} of 5.8 μM for CKD9/cyclin T1. FIT-039 does not inhibit other CDKs and other kinases. FIT-039 inhibits replication of HSV-1 (IC_{50} of 0.69 μM), HSV-2, human adenovirus, and human CMV. FIT-039 is a promising antiviral agent for inhibiting drug-resistant HSVs and other DNA viruses.

IC_{50} & Target				
	CDK9/cyclinT1 5.8 μM (IC_{50})	HSV-1 0.69 μM (IC_{50})	HSV-2	CMV

In Vitro

FIT-039 (30 μM; 3 hours; HEK293 cells) treatment decreases phosphorylated CTD in the infected or noninfected cells to a

level lower than that shown by Flavopiridol. FIT-039 reduces the expression levels of HSV-1 immediate-early genes (IEGs) and early and late genes[1].

FIT-039 inhibits replication of the HSV-1 genome in a dose-dependent manner (EC_{50} and EC_{80} are 0.69 μM and 4.0 μM, respectively)[1].

FIT-039 potently suppresses 8 kinases (GSK3β, PKN1, haspin, p70s6K, DYRK1B, GSK3α, IRR, and DYRK3) other than CDK9 on the 332-kinase panel. These kinases are involved in the replication of various viruses[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	HEK293 cells
Concentration:	30 μM
Incubation Time:	3 hours
Result:	Decreased phosphorylated carboxyterminal domain (CTD) in the infected or noninfected cells to a level lower than that shown by Flavopiridol.

In Vivo

Treatment with the FIT-039 ointment twice a day suppresses skin lesions and rescues mice (male BALB/c mice injected with HSV-1) from lethality in a dose-dependent manner. The healing of lesions is observed with 5% to 10% FIT-039 ointment, leading to the complete regression of zosteriform spread on day 10, which is also observed with the 5% ACV ointment[1].

FIT-039 does not affect body weight gain in mice administrated with an overdose of this compound (1000 mg/kg/d) for 14 days, and no changes are observed in biological markers in their blood[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Makoto Yamamoto, et al. CDK9 Inhibitor FIT-039 Prevents Replication of Multiple DNA Viruses. J Clin Invest. 2014 Aug;124(8):3479-88.

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