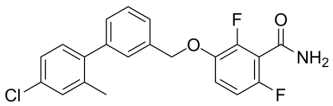
FtsZ-IN-4

Cat. No.:	HY-150754
CAS No.:	2882904-64-3
Molecular Formula:	$C_{21}H_{16}ClF_2NO_2$
Molecular Weight:	387.81
Target:	Bacterial
Pathway:	Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

FtsZ-IN-4 is an orally active FtsZ (filamenting temperature-sensitive mutant Z) inhibitor, exhibits excellent antibacterial activity. FtsZ-IN-4 shows good pharmaceutical properties with low cytotoxicity (CC_{50} >20 μg/mL)[1].

IC_{50} & Target

Target: Filamenting temperature-sensitive mutant Z (FtsZ)[1]

In Vitro

MIC: Minimum inhibition concentration; MBC: Minimum bactericidal concentration.

FtsZ-IN-4 (compound 30) shows potent antibacterial activity to B. subtilis and S. aureus with MICs of 0.008-0.25 μg/mL, respectively[1].

FtsZ-IN-4 (0.064 μg/mL or 0.5 μg/mL; 0-24 h) shows rapid bactericidal properties within 3 h, and the MBC/MIC ratios are ≤4, satisfying CLSI standards[1].

FtsZ-IN-4 (>20 μg/mL; 72 h) exerts low cytotoxicity towards Vero cells [1].

FtsZ-IN-4 (0.016 μg/mL; 3 h) increases the length of the B. subtilis ATCC9372, causes abnormal bacterial cell division and lead to bacterial cell death[1].

FtsZ-IN-4 (10 μg/mL; 0-15 min) induces SaFtsZ polymerization and (0-35 μg/mL; 30 min) inhibits the GTPase activity of SaFtsZ in a dose-dependent manner[1].

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

Cell Cytotoxicity Assay[1]

Cell Line:	Vero cells (African green monkey kidney cells)
Concentration:	>20 μg/mL
Incubation Time:	72 hours
Result:	Exhibited the 50% cytotoxic concentration (CC_{50}) >20 μg/mL, much more than the inhibition of B. subtilis ATCC9372 (MIC =0.016 μg/mL).

Cell Proliferation Assay[1]

Cell Line:	S. aureus ATCC25923 and Bacillus ATCC9372
Concentration:	1×, 2×, 4×, 8× MIC; MIC =0.125 μg/mL (S. aureus); 0.016 μg/mL (Bacillus)
Incubation Time:	3, 6, 12, 24 hours

Result:	Reduced B. subtilis ATCC9372 and S. aureus ATCC25923 cells below the lowest detectable limit (103 CFU/ mL) in 3 h.

In Vivo

FtsZ-IN-4 (compound 30) (5 mg/kg; p.o.) exhibits moderate exposure ($AUC_{(0-t)}$ =544.2 h*ng/mL) and an oral bioavailability (F) of 61.2% in mice[1].

FtsZ-IN-4 (25 mg/kg; i.v.) exerts good in vivo efficacy in mice.Murine pharmacokinetic profiles of FtsZ-IN-4[1]

Route	Dose (mg/kg)	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	$AUC_{(0-t)}$ (h•ng/mL)	$AUC_{(0-\infty)}$ (h•ng/mL)	V_{ss} (ng/mL)	CL (mL/h/kg)	F (%)
i.v.	1	0.28	0.083	480.5	177.8	178.7	1545.5	5682.8	/
5	2.26	0.5	429.3	544.2	559.3	/	/	61.2	

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

Animal Model:	Male ICR mice (infected with S. aureus ATCC25923)[1]
Dosage:	25 mg/kg
Administration:	Intraperitoneal injection; 0.5 mL
Result:	Significantly reduced the bacteria burden and showed comparable in vivo efficacy with vancomycin.

REFERENCES

[1]. Deng J, et al. Design, synthesis and biological evaluation of biphenyl-benzamides as potent FtsZ inhibitors. Eur J Med Chem. 2022 Sep 5. 239:114553.

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