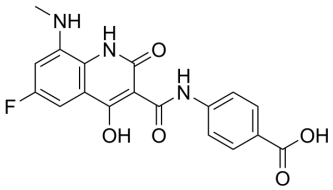
TP0480066

Cat. No.:	HY-150045
CAS No.:	2245693-15-4
Molecular Formula:	$C_{18}H_{14}FN_3O_5$
Molecular Weight:	371.32
Target:	Topoisomerase; Bacterial
Pathway:	Cell Cycle/DNA Damage; Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

TP0480066 is a selective topoisomerase II inhibitor with IC_{50}s of 1.10 and 62.89 nM for DNA gyrase and topo IV, respectively. TP0480066 shows good activity of againsting various bacterial species including drug-resistant strains. TP0480066 also exhibits potent inhibitory activity to N. gonorrhoeae, can be used in study of gonorrhea[1][2].

IC_{50} & Target	Topoisomerase II	DNA gyrase 1.10 nM (IC_{50})	topo IV 62.89 nM (IC_{50})

In Vitro

TP0480066 (compound 32) (0-2048 μg/mL; 18-24 h) demonstrats favorable antimicrobial activities against various bacterial species including some clinically isolated drug-resistant strains : MRSA (n=24), gPRSP (n=30), and VRE (n=34)[1].
TP0480066 (0-2048 μg/mL; 18-24 h) shows good antibacterial activity against Clostridioides difficile[1].
TP0480066 (0-2048 μg/mL; 24-48 h) demonstrates potent antibacterial activity to N. gonorrhoeae, including strains with decreased susceptibility or resistance to currently available antimicrobial agents[2].
TP0480066 (1.25×10^{-4}, 5×10^{-4} and 2×10^{-3} μg/mL; 24 h) shows good time-kill activity when concentration up to (or more than) MIC (5×10^{-4} μg/mL) in N. gonorrhoeae ATCC 49226[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	Clinically isolated Methicillin-resistant S. aureus (24 strains), Vancomycin-resistant enterococci (E. faecium (29 strains) and E. faecalis (5 strains), vanA positive (18 strains), vanB positive (14 strains) and vanA/vanB negative (2 strains)), Genotype penicillin-resistant S. pneumonia (30 strains)
Concentration:	0-2048 μg/mL
Incubation Time:	18-24 h
Result:	Showed favorable antimicrobial activities to drug-resistant strains with MIC ranges of 0.03-0.5, 0.015-0.25 and 0.002-0.015 μg/mL for MRSA (n=24), gPRSP (n=30), and VRE (n=34), respectively.

Cell Viability Assay[2]

Cell Line:	N. gonorrhoeae ATCC (49226, 43069, BAA-1846, 700717, 700825), N. gonorrhoeae NCTC (13477, 13478, 13479, 13480, 13481, 13482, 13483, 13818, 13821)

Concentration:	0-2048 μg/mL
Incubation Time:	24-48 h
Result:	Exhibited significant antimicrobial activities to both N. gonorrhoeae and drug-resistant N. gonorrhoeae (MIC ranges both were ≤0.00012-0.0005 μg/mL)

Cell Viability Assay[2]

Cell Line:	N. gonorrhoeae ATCC 49226
Concentration:	1.25×10^{-4}, 5×10^{-4} and 2×10^{-3} μg/mL
Incubation Time:	24 h
Result:	Reduced the viable N. gonorrhoeae ATCC 49226 counts by more than 3-$\log_{10}$ CFU/mL (99.9%) after 6 h at 4× MIC and after 24 h at the MIC, respectively.

In Vivo

TP0480066 (100 mg/kg; s.c; once) demonstrates C_{max}, T_{max}, $t_{1/2}$, and $AUC_{0\text{-}24\ h}$ values of 12400 ng/mL, 0.250 h, 6.79 h, 16000 h•ng/mL, respectively[2].

TP0480066 (1, 3, 10, 30, 100 mg/kg; s.c.; single) inhibits (30, 100 mg/kg) both N. gonorrhoeae ATCC 49226 and NCTC 13479 at 24 h and in a dose-dependent manner in mice[2].

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

Animal Model:	Female Slc:ICR mice[1]
Dosage:	100 mg/kg
Administration:	Subcutaneous injection, once.
Result:	Pharmacokinetic Parameters of TP0480066 in Female Slc:ICR mice (n=3)[1].

	T_{max} (h)	C_{max} (ng/mL)	$AUC_{0\text{-}24}$ (ng/mL•h)	$t_{1/2}$ (h)
SC (100 mg/kg)	0.250	12400	16000	6.79

Animal Model:	Female BALB/c mice (6-week-old; genital tract infection model)[2]
Dosage:	1, 3, 10, 30 and 100 mg/kg
Administration:	Subcutaneous administration; single.
Result:	Significantly decreased mean viable cell counts of N. gonorrhoeae ATCC 49226 and NCTC 13479 when at 30, 100 mg/kg.

REFERENCES

[1]. Ushiyama F, et al. Lead optimization of 8-(methylamino)-2-oxo-1,2-dihydroquinolines as bacterial type II topoisomerase inhibitors. Bioorg Med Chem. 2020 Nov 15;28(22):115776.

[2]. Masuko A, et al. In Vitro and In Vivo Activities of TP0480066, a Novel Topoisomerase Inhibitor, against Neisseria gonorrhoeae. Antimicrob Agents Chemother. 2021 Mar 18;65(4):e02145-20.

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