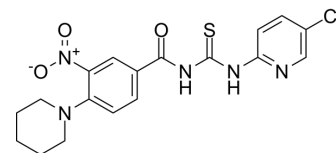


## MAC-545496

Cat. No.:	HY-130613		
CAS No.:	838810-96-1		
Molecular Formula:	C <sub>18</sub> H <sub>18</sub> ClN <sub>5</sub> O <sub>3</sub> S		
Molecular Weight:	419.89		
Target:	Bacterial		
Pathway:	Anti-infection		
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 : 250 mg/mL (595.39 mM; Need ultrasonic)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.3816 mL	11.9079 mL	23.8158 mL
	5 mM	0.4763 mL	2.3816 mL	4.7632 mL
	10 mM	0.2382 mL	1.1908 mL	2.3816 mL

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

### BIOLOGICAL ACTIVITY

#### Description

MAC-545496 is a nanomolar inhibitor of glycopeptide-resistance-associated protein R (GraR). MAC-545496 displays strong binding affinity to the full-length GraR protein ( $K_D \leq 0.1$  nM). MAC-545496 is an antivirulence agent that reverses  $\beta$ -lactam resistance in Methicillin-resistant strains (MRSA)<sup>[1]</sup>.

#### IC<sub>50</sub> & Target

Glycopeptide-resistance-associated protein R (GraR)<sup>[1]</sup>

#### In Vitro

MAC-545496 potently synergizes with Cefuroxime; concentrations as low as 0.03  $\mu$ g/mL (~75 nM) lowers the  $\beta$ -lactam MIC from 512 to 8  $\mu$ g/mL against *S. aureus* USA300. MAC545496 also synergizes with Cefuroxime and Oxacillin against a collection of ten *S. aureus* clinical isolates. In addition, MAC-545496 potentiates the effect of Cefuroxime against representatives of other circulating MRSA strains such as USA100, USA400 and USA500 to different extents, with the exception of CMRSA4, a USA200/EMRSA16 isolate. MAC-545496 also synergizes with the antimicrobial peptides colistin and polymyxin B<sup>[1]</sup>.

MAC-545496 shows inhibition of mprF expression in a concentration-dependent manner; the IC<sub>50</sub> value is 0.0376  $\mu$ g/mL<sup>[1]</sup>.

MAC-545496 also inhibits the citrate-induced biofilm formation in the wild type in a concentration dependent manner<sup>[1]</sup>.

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

#### In Vivo

In vivo, MAC-545496 is effective as a monotherapy for MRSA infected *Galleria mellonella* larvae. MAC-545496 activity is evidenced by increased survival of the drug-treated larvae as compared to infected untreated ones. This corresponded to concentration-dependent killing of *S. aureus* in the hemolymph of the larvae observed from the CFUs recovered from the hemolymph 200 min after infection. Treatment of *S. aureus*-infected larvae with MAC-545496 occurred 30min after infection that mimics acquiring bacterial infection before initiating antimicrobial therapy [1].  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### REFERENCES

[1]. El-Halfawy OM, et al. Discovery of an antivirulence compound that reverses  $\beta$ -lactam resistance in MRSA. *Nat Chem Biol*. 2019 Nov 25.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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