Product Data Sheet

Product Name: P005672 hydrochloride
Cat. No.: GC17232

Chemical Properties

Cas. No.	1035979-44-2		
Chemical Name	(4S,4aS,5aR,12aS)-4-(dimethylamino)-3,10,12,12a-tetrahydroxy-7-((methoxy(methyl)amino)methyl)-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carbimidic acid hydrochloride		
SMILES	CN([C@@]1([H])[C@]2([H])C[C@](C3=C(O)[C@]2(O)C(C(C(O)=N)=C1O)=O)([H])CC4=C(CN(OC)C)C=CC(O)=C4C3=O)C.Cl		
Formula	$C_{24}H_{30}ClN_3O_8$	M.Wt	523.96
Solubility	DMF: 0.25 mg/ml,DMSO: 0.25 mg/ml	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	P005672 hydrochloride		

Protocol

Cell experiment [1]:

Cell lines	Anaerobic Bacteria and Yeasts

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Preparation Method	1. Anaerobic Bacteria Minimum inhibitory concentration (MIC) testing was performed for anaerobic bacteria using a modified Clinical Laboratory Standards Institute (CLSI) M11-A7 agar dilution method in an anaerobic chamber. Bacteria were grown on Brucella Blood Agar plates supplemented with hemin and vitamin K, and infused with various concentrations of P005672 hydrochloride or minocycline (0.016-8μg/mL). Infused agar was inoculated with 2μL of 1 to 2 × 10^8 colony forming units (CFUs)/mL and incubated at 37°C for 48h in an anaerobic atmosphere. The lowest concentration of the antimicrobial agent that resulted in a visually evaluated inhibition of growth was recorded and MIC evaluated. 2. Yeasts *Candida* isolates were tested using a modified CLSI M27-A4 broth microdilution method at a range of 0.125–64μg/mL. RPMI 1640 broth was inoculated with 0.5 to 2.5 × 10^3 CFUs/mL, and incubated at 37°C for 24h. The lowest concentration of the antimicrobial agent that resulted in 50% growth inhibition when compared to the untreated growth control was recorded.
Reaction Conditions	0.016–8μg/mL or 0.125–64μg/mL; 48h or 24h
Applications	P005672 hydrochloride exhibited lower inhibitory activity against microbial species representing human gastrointestinal microbiota compared to minocycline.

Animal experiment [2]:

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Animal models	male Sprague Dawley rats
Preparation Method	To determine whether P005672 hydrochloride decreased inflammation, male Sprague Dawley rats were intraperitoneally injected with saline, P005672 hydrochloride, or a positive control (either doxycycline or minocycline), followed by a subplantar injection of sterile 1mg/0.1mL carrageenan solution in the right hind paw. Paw surface volume was measured immediately after carrageenan injection using a digital water plethysmometer, and again 3h later. Rats were euthanized via CO_2 asphyxiation followed by cervical dislocation immediately after the second measurement. Percent inflammation was calculated as 100 × ((paw volume at 3h-paw volume at 0h)/paw volume at 0h).
Dosage form	1, 5, 10, 25, 50, 75, 100 and 125mg/kg; 3h; i.p
Applications	In a rat paw edema model, the anti-inflammatory activity of P005672 hydrochloride was comparable to doxycycline and minocycline.

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References:
[1] Ghannoum MA, Long L, Bunick CG, Del Rosso JQ, Gamal A, Tyring SK, McCormick TS, Grada A. Sarecycline Demonstrated Reduced Activity Compared to Minocycline against Microbial Species Representing Human Gastrointestinal Microbiota. Antibiotics (Basel). 2022 Feb 28;11(3):324.
[2] Bunick CG, Keri J, Tanaka SK, Furey N, Damiani G, Johnson JL, Grada A. Antibacterial Mechanisms and Efficacy of Sarecycline in Animal Models of Infection and Inflammation. Antibiotics (Basel). 2021 Apr 15;10(4):439.

Background

P005672 hydrochloride is a novel, narrow-spectrum tetracycline derivative for the treatment of moderate to severe inflammatory non-nodular acne[1].

In vitro, P005672 hydrochloride (100μM; 25min) reduces *Staphylococcus aureus* DNA and protein synthesis[2]. P005672 hydrochloride exhibited lower inhibitory activity against microbial species representing human gastrointestinal microbiota compared to

minocycline[3].

In vivo, in a rat paw edema model, the anti-inflammatory activity of P005672 hydrochloride (1, 5, 10, 25, 50, 75, 100 and 125mg/kg; 3h; i.p.) was comparable to doxycycline and minocycline[2]. In a murine systemic (intraperitoneal) infection model, P005672 hydrochloride (0.25 mg/kg; 48h; s.c.) was effective in treating the systemic infection caused by *Staphylococcus aureus*, while P005672 hydrochloride (40 mg/kg; 48h; s.c.) did not demonstrate in vivo efficacy against the systemic infection caused by *Escherichia coli* PBS1478[4].

References:
[1] Kaul G, Saxena D, Dasgupta A, Chopra S. Sarecycline hydrochloride for the treatment of acne vulgaris. Drugs Today (Barc). 2019 Oct;55(10):615-625. doi: 10.1358/dot.2019.55.10.3045040. PMID: 31720559.
[2] Bunick CG, Keri J, Tanaka SK, Furey N, Damiani G, Johnson JL, Grada A. Antibacterial Mechanisms and Efficacy of Sarecycline in Animal Models of Infection and Inflammation. Antibiotics (Basel). 2021 Apr 15;10(4):439.
[3] Ghannoum MA, Long L, Bunick CG, Del Rosso JQ, Gamal A, Tyring SK, McCormick TS, Grada A. Sarecycline Demonstrated Reduced Activity Compared to Minocycline against Microbial Species Representing Human Gastrointestinal Microbiota. Antibiotics (Basel). 2022 Feb 28;11(3):324.
[4] Zhanel G, Critchley I, Lin LY, Alvandi N. Microbiological Profile of Sarecycline, a Novel Targeted Spectrum Tetracycline for the Treatment of Acne Vulgaris. Antimicrob Agents Chemother. 2018 Dec 21;63(1):e01297-18.

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