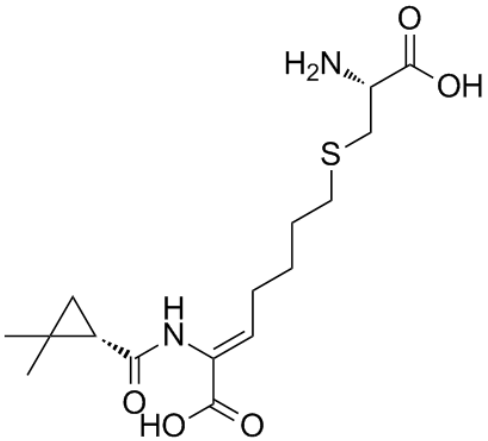
Product Data Sheet

Product Name: Cilastatin (MK0791)
Cat. No.: GC32162

Chemical Properties

Cas. No.	82009-34-5		
SMILES	O=C(O)/C(NC([C@@H]1C(C)(C)C1)=O)=C/CCCCSC[C@H](N)C(O)=O		
Formula	$C_{16}H_{26}N_2O_5S$	M.Wt	358.45
Solubility	DMSO : 15 mg/mL (41.85 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C 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



Protocol

Cell experiment [1]:

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Cell lines	Renal Proximal Tubular Primary Cell (RPTECs)
Preparation Method	In all the assays RPTECs were treated with 10, 20 and 30mg/mL of gentamicin in the presence or absence of Cilastatin (200μg/mL) for 24h.
Reaction Conditions	200μg/mL; 24h
Applications	The treatment with gentamicin induces dose-dependent apoptosis in RPTECs, and this process can be rescued by Cilastatin.

Animal experiment [2]:

Animal models	C57BL/6J mice
Preparation Method	The experimental protocol used in this study was approved by the animal experiments ethics committee of our institution. We housed male C57BL/6J mice that weighed approximately 22 to 24g under a 12-h light–dark cycle, and food and water were freely available. We used seven groups of mice in this experiment (control, Cilastatin 150mg/kg/day, Cilastatin 300mg/kg/day, vancomycin (VCM) 400mg/kg/day + Cilastatin 150mg/kg/day, VCM 400mg/kg/day + Cilastatin 300mg/kg/day, VCM 600mg/kg/day + Cilastatin 150mg/kg/day, VCM 600mg/kg/day + Cilastatin 300mg/kg/day), and each group consisted of eight mice. We injected the VCM and Cilastatin intraperitoneally for 7 consecutive days, and the control group received the same volume of sterile distilled water.
Dosage form	150-300mg/kg/day; 7 days; i.p

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Applications	Cilastatin 300 mg/kg treatment significantly decreased the vancomycin concentrations in the blood and kidney.

References:
[1] Jado, Juan Carlos et al. “Nephroprotective Effect of Cilastatin against Gentamicin-Induced Renal Injury In Vitro and In Vivo without Altering Its Bactericidal Efficiency.” *Antioxidants (Basel, Switzerland)* vol. 9,9 821. 3 Sep. 2020, doi:10.3390/antiox9090821
[2] Im, Dai Sig et al. “Cilastatin attenuates vancomycin-induced nephrotoxicity via P-glycoprotein.” *Toxicology letters* vol. 277 (2017): 9-17. doi:10.1016/j.toxlet.2017.05.023

Background

Cilastatin (MK0791) is a reversible, competitive renal dehydropeptidase I (DHP-I) inhibitor with an IC_{50} of 0.1μM *in vitro*. Cilastatin is an antibacterial adjunct that inhibits the metallob-lactamase enzyme CphA and membrane dipeptidase (MDP) of bacteria with an IC_{50} of 178±11μM and 0.3±0.01μM, respectively[1,2]. Cilastatin shows protective effect against acute kidney injury caused by vancomycin-induced nephrotoxicity[3,4].

In vitro, Cilastatin (0.5μg/ml; up to 24h) inhibits the growth of a broad spectrum of both gram-positive and gram-negative bacteria such as Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae et.al with a lower IC_{50} compares to Imipenem, Ciprofloxacin, Amikacin, Ceftazidime, and Piperacillin[2]. Cilastatin (200μg/mL; 24h) shows a nephroprotective effect against gentamicin-induced renal injury without altering the bactericidal efficiency of gentamicin in vitro with a renal proximal tubular primary cell model[5]. Imipenem/Cilastatin (IPM/CS) (7.25mg/ml) combination demonstrates an embolic effect with a particle analysis[6].

In vivo, Cilastatin (150mg/kg/day; 7 days; i.p) attenuates vancomycin-induced nephrotoxicity via P-glycoprotein[7]. Cilastatin (200mg/kg; retroorbital injection) administration caused selective proteinuria and inhibition of tubular myoglobin uptake similar to that caused by a megalin deletion in a C57BL/6-based *in vivo* research[8].

References:

Product Data Sheet

[1] Keynan, S et al. “The renal membrane dipeptidase (dehydropeptidase I) inhibitor, cilastatin, inhibits the bacterial metallo-beta-lactamase enzyme CphA.” *Antimicrobial agents and chemotherapy* vol. 39,7 (1995): 1629-31. doi:10.1128/AAC.39.7.1629
[2] Petersen, P J et al. “In vitro and in vivo activities of LJC10,627, a new carbapenem with stability to dehydropeptidase I.” *Antimicrobial agents and chemotherapy* vol. 35,1 (1991): 203-7. doi:10.1128/AAC.35.1.203
[3] Humanes, Blanca et al. “Protective Effects of Cilastatin against Vancomycin-Induced Nephrotoxicity.” *BioMed research international* vol. 2015 (2015): 704382. doi:10.1155/2015/704382
[4] González-Nicolás, María Ángeles, and Alberto Lázaro. “Cilastatin, a new therapeutic promise for acute kidney injury.” *Kidney international* vol. 106,4 (2024): 560-562. doi:10.1016/j.kint.2024.07.024
[5] Jado, Juan Carlos et al. “Nephroprotective Effect of Cilastatin against Gentamicin-Induced Renal Injury In Vitro and In Vivo without Altering Its Bactericidal Efficiency.” *Antioxidants (Basel, Switzerland)* vol. 9,9 821. 3 Sep. 2020, doi:10.3390/antiox9090821
[6] Nakamura, Hiroki et al. “In vitro study of the embolic characteristics of imipenem/cilastatin particles.” *CVIR endovascular* vol. 7,1 27. 11 Mar. 2024, doi:10.1186/s42155-024-00441-x
[7] Im, Dai Sig et al. “Cilastatin attenuates vancomycin-induced nephrotoxicity via P-glycoprotein.” *Toxicology letters* vol. 277 (2017): 9-17. doi:10.1016/j.toxlet.2017.05.023
[8]Matsushita, Katsuyuki et al. “Cilastatin Ameliorates Rhabdomyolysis-induced AKI in Mice.” *Journal of the American Society of Nephrology : JASN*vol. 32,10 (2021): 2579-2594. doi:10.1681/ASN.2020030263

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