

Product Data Sheet

Product Name: MG-132
Cat. No.: GC10383

Chemical Properties

Cas. No. 133407-82-6

Chemical Name benzyl N-[(2S)-4-methyl-1-[[[(2S)-4-methyl-1-[[[(2S)-4-methyl-1-oxopentan-2-yl]amino]-1-oxopentan-2-yl]amino]-1-oxopentan-2-yl]carbamate

SMILES CC(C)CC(C=O)NC(=O)C(CC(C)C)NC(=O)C(CC(C)C)NC(=O)OCC1=CC=CC=C1

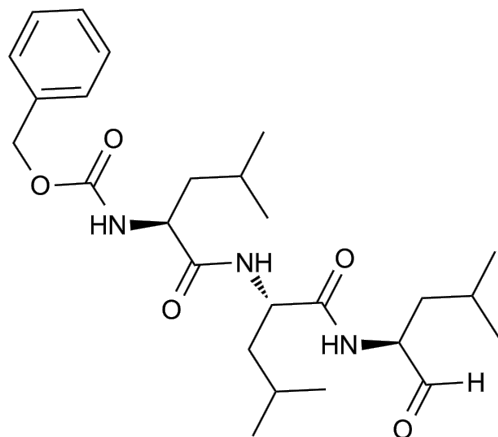
Formula $C_{26}H_{41}N_3O_5$ M.Wt 475.6

Solubility $\geq 23.78\text{mg/mL}$ in DMSO 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 KIM-2

MG-132 were diluted in Me2SO. Cells were treated with protease inhibitors or dilutant alone. Supernatant and monolayer cells were harvested by centrifugation Preparation Method and fixed in 70% ethanol in PBS for staining with acridine orange. Equal volumes of cells and acridine orange (5 mg/ml in PBS) were mixed on a microscope slide and examined by fluorescence microscopy.

Reaction Conditions 0, 1.5, 5 μ M, 24 h

Applications MG-132 treatment induces apoptosis in a cell cycle dependent manner.

Animal experiment [2]:

Animal models C57BL/10ScSn DMD mdx mice

Localized administration was performed by injection of MG-132 into the gastrocnemius muscles of mdx mice. To visualize the injected muscle, MG-132 (final concentration of 20 μ mol/L) was pre-mixed with 1% India ink in phosphate-buffered saline (PBS) for a total volume of 100 μ l. Mice were sacrificed 24 hours after injection, and skeletal muscles were quickly isolated for further analysis. To Preparation Method systemically administer MG-132, Alzet Minipumps was subcutaneously implanted in the anterior back region of mdx mice. Experiments were conducted on 6-month-old mdx mice. For 8 days, administration of either different concentrations of MG-132 (delivered at rate of either 1 μ g, or 5 μ g or 10 μ g/kg/24 hours) or the inhibitor-diluent (PBS only) was enforced, as a negative control. Skeletal muscle tissues were collected from untreated (PBS only) and MG-132-treated mdx mice for further analysis.

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Dosage form 1 µg, 5 µg, 10 µg/kg, injection into the gastrocnemius muscles or subcutaneously implanted Alzet Minipumps

Applications MG-132, as a proteasomal inhibitor, effectively rescues the expression levels and plasma membrane localization of dystrophin, β-dystroglycan, α-dystroglycan, and α-sarcoglycan in skeletal muscle fibers from mdx mice. Furthermore, MG-132 reduces muscle membrane damage, as revealed by vital staining of the diaphragm and gastrocnemius muscle isolated from treated mdx mice, and ameliorates the histopathological signs of muscular dystrophy, as judged by hematoxylin and eosin staining of muscle biopsies taken from treated mdx mice.

References:

- [1]. Tsubuki, S et al. Differential inhibition of calpain and proteasome activities by peptidyl aldehydes of di-leucine and tri-leucine. Journal of biochemistry vol. 119,3 (1996): 572-6.
- [2]. MacLaren, A P et al. p53-dependent apoptosis induced by proteasome inhibition in mammary epithelial cells. Cell death and differentiation vol. 8,3 (2001): 210-8.
- [3]. Bonuccelli, Gloria et al. Proteasome inhibitor (MG-132) treatment of mdx mice rescues the expression and membrane localization of dystrophin and dystrophin-associated proteins. The American journal of pathology vol. 163,4 (2003): 1663-75.

Background

MG-132 is a potent proteasome and calpain inhibitor with IC₅₀ values of 100nM and 1.25µM, respectively^[1]. MG-132 can cause upregulation of Nrf2-dependent antioxidative function and downregulation of NF-κB-mediated inflammation^[2]. MG-132 has been widely used to alleviate the progression of arthritis and pain in rats^[3].

In vitro, MG-132 treatment for 24 hours significantly inhibited the proliferation of C6 cells, with an

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IC₅₀ value of 18.5μM^[4]. Treatment with 1μM MG-132 for 24 hours significantly induced apoptosis in U87MG cells and A172 cells, accompanied by an increase in mitochondrial membrane potential and nuclear translocation of mitochondrial protein AIF^[5]. Treatment with 1μM MG-132 for 24 hours significantly inhibited DNA synthesis in SW1116 and HT-29 cells and activated the BMP signaling pathway, resulting in cell growth inhibition^[6].

In vivo, MG-132 treatment via intraperitoneal injection at a dose of 10μg/kg/day for 7 days significantly improved the cardiac function of the mouse model of myocarditis induced by Coxsackievirus B3 and inhibited the structural remodeling of the ventricle^[7]. A single intraperitoneal injection of MG-132 at a dose of 9mg/kg for 6 hours significantly mitigated the liver swelling, degeneration and inflammatory cell infiltration in the acute liver injury mouse model^[8].

References:

- [1] Tsubuki S, Saito Y, Tomioka M, et al. Differential inhibition of calpain and proteasome activities by peptidyl aldehydes of di-leucine and tri-leucine[J]. The journal of biochemistry, 1996, 119(3): 572-576.
- [2] Wang Y, Sun W, Du B, et al. Therapeutic effect of MG-132 on diabetic cardiomyopathy is associated with its suppression of proteasomal activities: roles of Nrf2 and NF-κB[J]. American Journal of Physiology-Heart and Circulatory Physiology, 2013, 304(4): H567-H578.
- [3] Ahmed A S, Ahmed M, Li J, et al. Proteasome inhibitor MG 132 modulates inflammatory pain by central mechanisms in adjuvant arthritis[J]. International journal of rheumatic diseases, 2017, 20(1): 25-32.
- [4] Fan W, Hou Y, Meng F, et al. Proteasome inhibitor MG-132 induces C6 glioma cell apoptosis via oxidative stress[J]. Acta Pharmacologica Sinica, 2011, 32(5): 619-625.
- [5] Ko J K, Choi C H, Kim Y K, et al. The proteasome inhibitor MG-132 induces AIF nuclear translocation through down-regulation of ERK and Akt/mTOR pathway[J]. Neurochemical research, 2011, 36(5): 722-731.
- [6] Wu W K K, Sung J J Y, Wu Y C, et al. Bone morphogenetic protein signalling is required for the anti-mitogenic effect of the proteasome inhibitor MG-132 on colon cancer cells[J]. British journal of

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pharmacology, 2008, 154(3): 632-638.

[7] Zhang X M, Li Y C, Chen P, et al. MG-132 attenuates cardiac deterioration of viral myocarditis via AMPK pathway[J]. Biomedicine & Pharmacotherapy, 2020, 126: 110091.

[8] Shan C, Ou D, Xiong Y, et al. Molecular mechanism of anti-inflammatory effects of the proteasome inhibitor MG-132 on Con A-induced acute liver injury in mice[J]. Research in Veterinary Science, 2023, 156: 60-65.

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