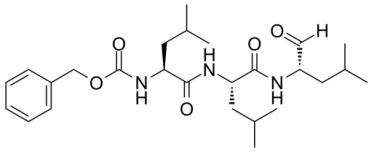
Data Sheet

Product Name:	MG-132
Cat. No.:	CS-0471
CAS No.:	133407-82-6
Molecular Formula:	C26H41N3O5
Molecular Weight:	475.62
Target:	Autophagy; Proteasome
Pathway:	Autophagy; Metabolic Enzyme/Protease
Solubility:	DMSO : 83.33 mg/mL (ultrasonic);H_2O : < 0.1 mg/mL



BIOLOGICAL ACTIVITY:

MG-132 is a potent, reversible **proteasome** inhibitor with an **IC_{50}** of 100 nM. MG-132 effectively blocks the proteolytic activity of the 26S proteasome complex. MG-132, a peptide aldehyde, is an **autophagy** activator[1][2]. IC50 & Target: IC50: 100 nM (Proteasome)[1] **In Vitro:** MG-132 (10-40 μM; 24 hours) significantly reduces the viability of C6 glioma cells in both time- and concentration-dependent manners and shows the IC_{50} of 18.5 μM at 24 hours[3].

MG-132 (18.5 μM; 24 hours) induces down-regulation of anti-apoptotic proteins Bcl-2 and XIAP and up-regulates expression of pro-apoptotic protein Bax and caspase-3[3]. **In Vivo:** MG-132 (1 mg/kg; i.v.; twice a week for 4 weeks) shows potent tumor inhibitory effect against mice bearing HeLa tumors[4].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [3]After growing on six-well plates (3×10^5 cells/well) for 24 h, C6 glioma cells are treated with either PBS (control) or 18.5 μM MG-132 for 3, 6, 12, or 24 h at 37°C. Cells are thoroughly scraped from the culture dishes with a cell scraper and washed with cold PBS. After centrifugation for 10 min at 800×g, the cell pellets are suspended in ice-cold buffer (50 mM Tris-HCl, pH 7.5, 20 μM ATP, 5 mM $MgCl_2$, 1 mM dithiothreitol, and 20% glycerol) and homogenized with a Pyrex glass microhomogenizer (20 strokes). The homogenate is centrifuged at 15 000×g for 10 min at 4°C to obtain supernatant. Protein concentration is determined using protein assay kits. A total of 10 μL (1 μg/μL) of each freshly made supernatant is incubated in a 96-well plate at 37°C for 30 min with 10 μL of 300 μM of Succinyl-LLVY-AMC and 85 μL of assay buffer (20 mM Tris-HCl, pH 7.5, and 20% glycerol). Release of fluorescent AMC is measured with a spectrofluorometer at 440 nm with an excitation wavelength of 380 nm[3]. **Cell Assay:** [3]C6 glioma cells are seeded onto 96-well microplates (3×10^4 cells/well) and cultured for 24 h. The cells are treated with PBS or MG-132 final concentrations of 10, 20, 30, and 40 μM, respectively. Cell viability is assessed using an MTT assay at 3, 6, 12, and 24 h after MG-132 treatment. The absorbance value at 570 nm is read using an automatic multi-well spectrophotometer. C6 glioma cells (3×10^5 cells/well) are allowed to grow on coverslips in 6-well culture plates for 24 h. The cells are then treated with either PBS (control) or 18.5 μM MG-132 at 37°C for 24 h. Cells growing on glass coverslips are fixed in methanol for 5 min at room temperature. The fixed cells are washed twice with PBS and then incubated with Hoechst 33342 for 5 min at room temperature and observed under a fluorescence microscope. Fragmented or condensed nuclei are scored as apoptotic[3]. **Animal Administration:** MG-132 is dissolved in vehicle (0.1% DMSO) (Rats)[5].[4][5]Mice[4]

C.B-17/Icr-scid/scidJcl mice are inoculated s.c. with HeLa, CaSki, or C33A (1×10^7 cells). Tumors are allowed to grow for 1 week. Mice are killed and tumors are removed. Tumors are then cut into 2-mm diameter pieces and s.c. transplanted in C.B-17/Icr-scid/scidJcl mice (n=6 per group). One week after inoculation, mice are treated with i.v. injection of saline (control), MG-132 (1 mg/kg/dose) twice a week for 4 weeks. The volume (V) of tumors is measured before every injection, as estimated using equation $V=a\times b^2/2$ where a and b are major and minor axes of the tumor measured by a caliper, respectively.

Rats[5]

Male Sprague-Dawley rats (8 weeks old, 180-230 g) are used to establish pressure-overload model. All animals are separated into four groups (10 rats per group): (i) vehicle-treated sham group; (ii) MG-132-treated sham group; (iii) vehicle-treated abdominal aortic banding (AAB) group; and (iv) MG-132-treated AAB group. AAB is created using a 5-0 suture tied twice around the abdominal aorta in which a 21-gauge needle is inserted. The needle is then retracted yielding a 70-80% constriction with an outer aortic diameter of ~0.8 mm. In the sham surgery rats, the same surgery is performed except the aorta is constricted. At Day 3 after the surgery, MG-132-treated rats are intraperitoneally injected with 0.1 mg/kg/day of MG-132 for 8 weeks. All control animals are injected with a corresponding volume of vehicle only (0.1% DMSO).

References:

[1]. Harhouri K, et al. MG132-induced progerin clearance is mediated by autophagy activation and splicing regulation. EMBO Mol Med. 2017 Sep;9(9):1294-1313.

[2]. Han YH, et al. The effect of MG132, a proteasome inhibitor on HeLa cells in relation to cell growth, reactive oxygen species and GSH. Oncol Rep. 2009 Jul;22(1):215-21.

[3]. Fan WH, et al. Proteasome inhibitor MG-132 induces C6 glioma cell apoptosis via oxidative stress. Acta Pharmacol Sin. 2011 May;32(5):619-25.

[4]. Matsumoto Y, et al. Enhanced efficacy against cervical carcinomas through polymeric micelles physically incorporating theproteasome inhibitor MG132. Cancer Sci. 2016 Jun;107(6):773-81.

[5]. Chen B, et al. MG132, a proteasome inhibitor, attenuates pressure-overload-induced cardiac hypertrophy in rats by modulation of mitogen-activated protein kinase signals. Acta Biochim Biophys Sin (Shanghai). 2010 Apr;42(4):253-8.

CAIndexNames:

L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]-

SMILES:

O=C(OCC1=CC=CC=C1)N[C@H](C(N[C@@H](CC(C)C)C(N[C@H](C([H])=O)CC(C)C)=O)=O)CC(C)C

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