Ixazomib citrate

Cat. No.: HY-10452

CAS No.: 1239908-20-3

Molecular Formula: $C_{20}H_{23}BCl_2N_2O_9$

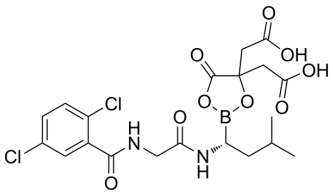
Molecular Weight: 517.12

Target: Proteasome; Autophagy

Pathway: Metabolic Enzyme/Protease; Autophagy

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 (483.45 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9338 mL	9.6689 mL	19.3379 mL
	5 mM	0.3868 mL	1.9338 mL	3.8676 mL
	10 mM	0.1934 mL	0.9669 mL	1.9338 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.02 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.02 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ixazomib citrate (MLN9708) is a reversible inhibitor of the chymotrypsin-like proteolytic β5 site of the 20S proteasome with an IC_{50} of 3.4 nM and a K_i of 0.93 nM.

IC_{50} & Target

IC50: 3.4 nM (20S proteasome β5), 31 nM (20S proteasome β1), 3500 nM (20S proteasome β2)[3]

In Vitro

Ixazomib citrate (MLN9708; 0.20-3.20 μM) inhibits the cell growth of both cell lines effectively in a time- and dose-dependent manner. Ixazomib induces cell cycle arrest in MG-63 and Saos-2 cells. Ixazomib induces apoptosis mainly through the

	caspases pathway and requires the activation of both caspase8 and caspase9. Ixazomib treatment increases the levels of pro-apoptotic proteins and down regulates the anti-apoptotic proteins that control MOMP. Ixazomib treatment induces the release of Cytc, Smac, OMI from mitochondria and decreases the protein levels of XIAP. Ixazomib inhibits the invasion ability of MG-63 and Saos-2 cells and decreases both the expression and secretion levels of MMP2/9[1].Ixazomib citrate (MLN9708; 12 nM) shows inhibitory activity against C-L and T-L proteasome activities. Treatment of H929 and MM.1S MM cells with Ixazomib triggers a marked increase in proteolytic cleavage of poly(ADP) ribose polymerase (PARP), a signature event during apoptosis. Ixazomib induces cleavage of caspase-3, an upstream activator of PARP. Ixazomib induces eIf2-α kinase activity and protein levels of Bip and CHOP/GADD153. Ixazomib blocks BMSCs-induced MM cell proliferation, inhibits in vitro capillary tubule formation, and target NF-κB[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ixazomib citrate (MLN9708; 11 mg/kg) significantly inhibits MM tumor growth and prolongs survival in the human plasmacytoma MM.1S xenograft mouse model. The blood chemistry profiles of Ixazomib-treated mice show normal levels of creatinine, hemoglobin, and bilirubin. Ixazomib dramatically increases the number of cleaved-caspase-3 positive cells of the xenograft model[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cell viability is assessed using the MTT assay. Cells are trypsinized and seeded in 96-well plate at 5000 cells per well. Cells are treated with Ixazomib or DMSO in basal medium at the indicated doses and times. Cell viability is determined relative to control cells treated with vehicle alone. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Ixazomib is dissolved in 5% 2-hydroxypropyl-β- cyclodextrin at 2 mg/mL concentration. The human plasmacytoma xenograft tumor model is used in the assay. CB-17 SCID mice (n=21) are subcutaneously inoculated with 5.0×10^6 MM.1S cells in 100 μL serum-free RPMI-1640 medium, and randomized to treatment groups when tumors reach 250-300 mm^3. Mice are treated with vehicle, bortezomib (1 mg/kg; i.v) or Ixazomib (11 mg/kg; i.v) twice weekly for 3 weeks. Animals are euthanized when their tumors reach 2 cm^3. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Chem Biol. 2021 Aug 30;S2451-9456(21)00393-7.
- J Med Chem. 2022 Jul 27.
- Research Square Preprint. 2022 Feb.
- Patent. US20220054606A1.

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REFERENCES

[1]. Liu R, et al. A New Perspective for Osteosarcoma Therapy: Proteasome Inhibition by MLN9708/2238 Successfully Induces Apoptosis and Cell Cycle Arrest and Attenuates the Invasion Ability of Osteosarcoma Cells in Vitro. Cell Physiol Biochem. 2017 Jan 27;41(2

[2]. Chauhan D, et al. In vitro and in vivo selective antitumor activity of a novel orally bioavailable proteasome inhibitor MLN9708 against multiple myeloma cells. Clin Cancer Res. 2011 Aug 15;17(16):5311-21.

[3]. Kupperman E, et al. Evaluation of the proteasome inhibitor MLN9708 in preclinical models of human cancer. Cancer Res. 2010 Mar 1;70(5):1970-80.

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