Carfilzomib

Cat. No.: HY-10455

CAS No.: 868540-17-4

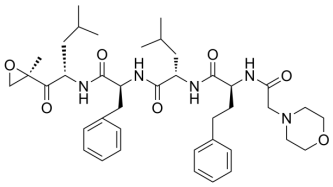
Molecular Formula: $C_{40}H_{57}N_5O_7$

Molecular Weight: 719.91

Target: Proteasome; Autophagy; Apoptosis

Pathway: Metabolic Enzyme/Protease; Autophagy; Apoptosis

Storage: Powder -20°C 3 years
4°C 2 years
* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (173.63 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.3891 mL	6.9453 mL	13.8906 mL
	5 mM	0.2778 mL	1.3891 mL	2.7781 mL
	10 mM	0.1389 mL	0.6945 mL	1.3891 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: 2.5 mg/mL (3.47 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.47 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.5 mg/mL (3.47 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Carfilzomib (PR-171) is an irreversible proteasome inhibitor with an IC_{50} of 5 nM in ANBL-6 and RPMI 8226 cells.

IC_{50} & Target

IC50: 5 nM (Proteasome)

In Vitro

Carfilzomib displays preferential in vitro inhibitory potency against the ChT-L activity in the β5 subunit, with over 80% inhibition at doses of 10 nM and above and little or no effect on the PGPH and T-L activities at doses up to 100 nM. Carfilzomib decreases the viability of ANBL-6, RPMI 8226 cells, U266 and KAS-6/1 cells with an IC_{50} less than 5 nM. Carfilzomib overcome Dex resistance, in that MM1.R cells reveals an IC_{50} of 15.2 nM, less than the value of 29.3 nM for

	parental MM1.S cells[1]. Co-treatment with carfilzomib and HDACIs leads to synergistic induction of cell death in various mantle cell lymphoma lines and primary mantle cell lymphoma cells. Combined treatment with carfilzomib or ONX0912 with vorinostat in HF-4B and Granta cells sharply increases caspase activation, PARP cleavage, JNK activation, MnSOD2 induction, and DNA damage[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Carfilzomib (2.0 mg/kg, i.v.) in conbination with 70 mg/kg vorinostat virtually abrogates tumor growth in Granta-luciferace cell xenograft flank model. Combined treatment results in a pronounced reduction in bioluminescence compared to animals treated with single agents or controls with minimal toxicity[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	WST-1 is used to determine the effects of proteasome inhibitors on cell proliferation according to the manufacturer's protocol. The inhibition of proliferation is calculated in relation to parallel control cells that receive vehicle alone and tabulated in KaleidaGraph 3.0.1 or Excel 2000. A linear spline function is used to interpolate the median inhibitory concentration (IC_{50}) using XLfit 4 software. The degree of resistance (DOR) is calculated using the formula: DOR=IC_{50} (resistant cells)/IC_{50}(sensitive cells). MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Animal studies are performed utilizing Beige-nude-XID mice. 10×10^6 Granta514 cells are pelleted, washed twice with 1X PBS, injected subcutaneously into the right flank. Once the tumors are visible, 5 to 6 mice are treated with carfilzomib±vorinostat and progress of tumor growth or regression is monitored. Stock vorinostat and carfilzomib is dissolved in DMSO and 10% sulfobutylether betacyclodextrin in 10 mM citrate buffer pH respectively. They are stored in −80°C in small aliquots and diluted before injection. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Drug Resist Updat. 2024 Jan 9, 101040.
- Nat Commun. 2020 Sep 4;11(1):4417.
- Mol Cell. 2022 Dec 20;S1097-2765(22)01137-6.
- Biomaterials. 16 September 2022.
- Cell Chem Biol. 2020 Dec 31;S2451-9456(20)30513-4.

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REFERENCES

[1]. Kuhn DJ, et al. Potent activity of carfilzomib, a novel, irreversible inhibitor of the ubiquitin-proteasome pathway, against preclinical models of multiple myeloma. Blood. 2007 Nov 1;110(9):3281-90.

[2]. Dasmahapatra G, et al. Carfilzomib interacts synergistically with histone deacetylase inhibitors in mantle cell lymphoma cells in vitro and in vivo. Mol Cancer Ther. 2011 Sep;10(9):1686-97.

Caution: Product has not been fully validated for medical applications. For research use only.

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