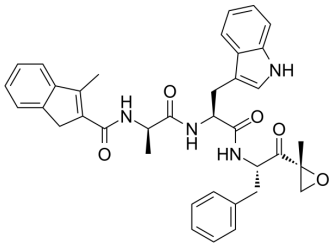
PR-924

Cat. No.:	HY-123587
CAS No.:	1416709-79-9
Molecular Formula:	$C_{37}H_{38}N_4O_5$
Molecular Weight:	618.72
Target:	Proteasome; Apoptosis
Pathway:	Metabolic Enzyme/Protease; Apoptosis
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 : 50 mg/mL (80.81 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6162 mL	8.0812 mL	16.1624 mL
	5 mM	0.3232 mL	1.6162 mL	3.2325 mL
	10 mM	0.1616 mL	0.8081 mL	1.6162 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 (4.04 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.04 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PR-924 is a selective tripeptide epoxyketone immunoproteasome subunit LMP-7 inhibitor with an IC_{50} of 22 nM. PR-924 covalently modifies proteasomal N-terminal threonine active sites. PR-924 inhibits growth and triggers apoptosis in multiple myeloma (MM) cells. PR-924 has antitumor activities[1][2].

IC_{50} & Target

IC50: 22 nM (LMP7), 8.2 μM (LMP2)[2]

In Vitro

PR-924 (1-20 μM; 24-72 hours; MM.1S, MM.1R, RPMI-8226, KMS12, LR-5, DOX40, INA-6, OPM1 and OPM2 cells) treatment significantly decreases the viability of all the MM cell lines in a time-and dose-dependent manner (IC_{50} range for cell lines: 3-7 μM for 48 h)[1].

PR-924 (3 μM; 48 hours; MM.1S and MM.1R cells) treatment triggers apoptosis in MM cells[1].

PR-924 (3 μM; 48 hours; MM.1S and MM.1R cells) treatment triggers activation of caspase-3, caspase-8 and caspase-9, and significantly down-regulated the expression of Bcl-2 protein, without altering Bax or MCL-1 protein levels[1].
PR-924 induces BID cleavage and its translocation to mitochondria, as well as cyto-c release BID, a proapoptotic BH-3 family protein, is linked to mitochondria-mediated apoptotic signaling pathways via cyto-c release[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	MM.1S, MM.1R, RPMI-8226, KMS12, LR-5, DOX40, INA-6, OPM1 and OPM2 cells
Concentration:	1-20 μM
Incubation Time:	24 hours, 48 hours, and 72 hours
Result:	Significantly decreased the viability of all the MM cell lines in a time-and dose-dependent manner (IC_{50} range for cell lines: 3-7 μM for 48 h).

Apoptosis Analysis[1]

Cell Line:	MM.1S and MM.1R cells
Concentration:	3 μM
Incubation Time:	48 hours
Result:	Triggered a significant increase in the Annexin V+/PI-apoptotic cell population.

Western Blot Analysis[1]

Cell Line:	MM.1S and MM.1R cells
Concentration:	3 μM
Incubation Time:	48 hours
Result:	Triggered activation of caspase-3, caspase-8 and caspase-9, and significantly down-regulated the expression of Bcl-2 protein.

In Vivo

PR-924 (6 mg/kg; intravenous injection; twice a week; for 21 days; CB-17 SCID-mice) treatment significantly inhibits tumour growth in human plasmacytoma xenografts[1].
PR-924 treatment significant reduces the shIL-6R levels in SCID-hu model. Treatment of tumour-bearing mice with PR-924, prolongs survival[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	CB-17 SCID-mice injected with MM.1S cells[1]
Dosage:	6 mg/kg
Administration:	Intravenous injection; twice a week; for 21 days
Result:	Inhibited tumour growth in human plasmacytoma xenografts.

REFERENCES

[1]. Singh AV, et al. PR-924, a selective inhibitor of the immunoproteasome subunit LMP-7, blocks multiple myeloma cell growth both in vitro and in vivo. Br J Haematol. 2011 Jan;152(2):155-63.

[2]. Parlati F, et al. Carfilzomib can induce tumor cell death through selective inhibition of the chymotrypsin-like activity of the proteasome. Blood. 2009 Oct 15;114(16):3439-47.

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