# PR-924

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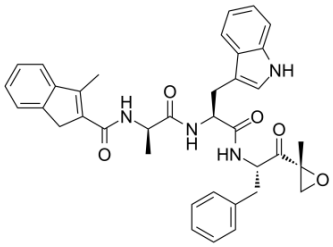
| **Cat. No.:** | HY-123587 |
| **CAS No.:** | 1416709-79-9 |
| **Molecular Formula:** | $C_{37}H_{38}N_4O_5$ |
| **Molecular Weight:** | 618.72 |
| **Target:** | Proteasome; Apoptosis |
| **Pathway:** | Metabolic Enzyme/Protease; Apoptosis |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |



## BIOLOGICAL ACTIVITY

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| **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]

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| 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]

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| 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]

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| 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.

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| 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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