Verucopeptin

Cat. No.:	HY-P2657
CAS No.:	138067-14-8
Molecular Formula:	$C_{43}H_{73}N_7O_{13}$
Molecular Weight:	896.08
Sequence Shortening:	L-{Aaa}-G-{Sar}-G-{Sar} Lactone:(Leu1-Sar6)
Target:	HIF/HIF Prolyl-Hydroxylase; Proton Pump; Endogenous Metabolite
Pathway:	Metabolic Enzyme/Protease; Membrane Transporter/Ion Channel
Storage:	Powder -80°C 2 years -20°C 1 year In solvent -80°C 6 months -20°C 1 month

BIOLOGICAL ACTIVITY

Description	Verucopeptin is a potent HIF-1 (IC_{50}=0.22 μM) inhibitor and decreases the expression of HIF-1 target genes and HIF-1α protein levels[1][2]. Verucopeptin strongly inhibits v-ATPase activity by directly targeting the v-ATPase ATP6V1G subunit but not ATP1V1B2 or ATP6V1D. Verucopeptin exhibits antitumor activity against multidrug resistance (MDR) cancers and can be used for cancer research[3].
IC_{50} & Target	IC50: 0.22 μM (HIF-1)[2] IC50: v-ATPase ATP6V1G subunit[3]
In Vitro	ATP6V1G, a subunit of the vacuolar H^+-ATPase (v-ATPase)[3]. Verucopeptin (0-30 μM; 72 h) shows excellent antitumor activity against K562R cells, with an IC_{50} of 388 nM, although these cells exhibit resistance to some other chemotherapeutic agents, such as Taxol and vincristine at concentrations of 10 μM[3]. Verucopeptin (0-1 μM) shows broad antiproliferative activity, with IC_{50} values of less than 100 nM against 66% of the cell lines evaluated among a total of 1,094 cancer cell lines. Moreover,Verucopeptin displays tissue specificity, such as leukemia, lymphoma, and melanoma, are classified in the lower IC_{50} groups, while the higher IC_{50} groups including other cancer types, such as non-small cell lung cancer[3]. Verucopeptin (10 nM; 1 hour) pretreatment blocks VE-P labeling of ATP6V1G1 but not ATP1V1B2 or ATP6V1D in a competitive binding assay. Verucopeptin shows substantial inhibition of v-ATPase activity and suppresses lysosomal acidification in vitro, as does Baf A1, although to a lesser extent[3]. Verucopeptin (0-500 nM; 1 hour) exhibits substantial inhibition of p-S6K as well as p-4EBP1 at concentrations of 10-200 nM. Additionally, Verucopeptin attenuates the phosphorylation of most of the tested mTORC1 downstream substrates, including p-4EBP1, $pmTOR^{S2448}$, $p\text{-}mTOR^{S2481}$, p-Rictor, p-ULK1, and p-Grb10, at concentrations ranging from 50 nM to 500 nM[3]. Verucopeptin (0-335 nM; 24 hour) decreases the HIF-1 protein level in a dose-dependent manner but has no effects on c-Raf in HT1080 cells. However, the known hsp90 inhibitor Tanespimycin (HY-10211) inhibits both HIF-1 and c-Raf expression in cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Verucopeptin (intravenous injection; 1 mg/kg; twice daily; 7 days) substantially represses tumor growth without significant body weight loss or gross signs of toxicity. HE staining indicated that Verucopeptin potently induces cell death and abrogates mTORC1 signaling by dephosphorylation of S6K and 4EBP1[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	BALB/c nude mice by subcutaneous injection of SGC7901/VCR cells[3]
Dosage:	1 mg/kg
Administration:	Intravenous injection; 1 mg/kg; twice daily; 7 days
Result:	Exhibited profound antitumor efficacy in vivo against MDR tumors.

REFERENCES

[1]. Aya Yoshimura, et al.Structure Elucidation of Verucopeptin, a HIF-1 Inhibitory Polyketide-Hexapeptide Hybrid Metabolite from an Actinomycete. Org Lett. 2015 Nov 6;17(21):5364-7.

[2]. Nobuaki Takahashi, et al. Total synthesis of verucopeptin, an inhibitor of hypoxia-inducible factor 1 (HIF-1). Chem Commun (Camb). 2019 Oct 1;55(79):11956-11959.

[3]. Yuezhou Wang, et al. Pharmacological Targeting of Vacuolar H +-ATPase via Subunit V1G Combats Multidrug-Resistant Cancer. Cell Chem Biol. 2020 Jun 30;S2451-9456(20)30234-8.

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