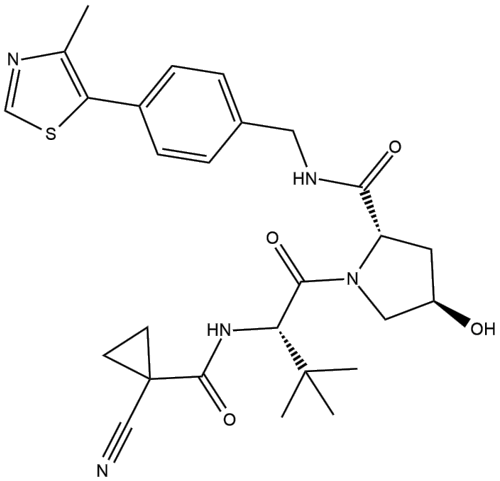
Product Data Sheet

Product Name: VH-298
Cat. No.: GC19375

Chemical Properties

Cas. No.	2097381-85-4		
SMILES	O=C([C@H]1N(C([C@H](C(C)(C)C)NC(C2(CC2)C#N)=O)=O)C[C@H](O)C1)NCC3=CC=C(C4=C(C)N=CS4)C=C3		
Formula	$C_{27}H_{33}N_5O_4S$	M.Wt	523.65
Solubility	DMSO : ≥ 83.3 mg/mL (159.08 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines	HeLa cells (human epithelial immortal cell line) and RPE/mRFP-EGFP-SKL cells (hTERT RPE-1 cells stably expressing monomeric red fluorescent protein-enhanced green fluorescent protein-serine-lysine-leucine)

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Preparation Method	HeLa cells and RPE/mRFP-EGFP-SKL cells were maintained in Dulbecco's minimal essential medium (DMEM) supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin at 37 °C under 5% CO_2. Cells were treated with VH-298 (50μM).
Reaction Conditions	50μM; 48h
Applications	VH-298 promoted peroxisomal degradation (pexophagy) in an ATG5-dependent manner, increased ubiquitination of the peroxisomal membrane protein ABCD3, and required NBR1. VH-298-induced pexophagy was mediated through activation of HIF-1α transcriptional activity.

Animal experiment [2]:

Animal models	Sprague-Dawley rats with streptozotocin-induced hyperglycaemia
Preparation Method	A full-thickness excisional wound (8mm) was created on the dorsal back of each rat. Rats were treated with VH-298 or PBS by local injection into the wound area every three days. Wound tissues were harvested at postoperative days 7, 14, and 21 for histological analysis.
Dosage form	30μM in 100μl; local injection; every three days for 21 days

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Applications	VH-298 treatment accelerated wound healing, improved healing pattern, increased granulation tissue area, enhanced collagen accumulation, promoted angiogenesis (more CD31-positive cell clusters), and activated the HIF-1 signalling pathway (increased HIF-1α, hydroxy-HIF-1α, and VEGF-A positive cells) in the wound area.

References:
[1] Kim YH, Park NY, Jo DS, et al. Inhibition of VHL by VH298 Accelerates Pexophagy by Activation of HIF-1α in HeLa Cells. Molecules. 2024 Jan 18;29(2):482.
[2] Qiu S, Jia Y, Sun Y, et al. Von Hippel-Lindau (VHL) Protein Antagonist VH298 Improves Wound Healing in Streptozotocin-Induced Hyperglycaemic Rats by Activating Hypoxia-Inducible Factor-(HIF-) 1 Signalling. J Diabetes Res. 2019 Feb 17;2019:1897174.

Background

VH-298 is a selective VHL (Von Hippel-Lindau) inhibitor (K_d=80-90nM). VH-298 stabilizes HIF-α proteins and triggers a hypoxic response by blocking the interaction between VHL and HIF-α proteins. VH-298 can be used in PROTAC (Proteolysis Targeting Chimera) technology and research related to hypoxia signaling pathways[1-4].

In vitro, VH-298 (30-100μM) was used to treat $CD4^+$ T cells under Th17-polarizing conditions for 72 hours. VH-298 increased HIF-1α protein levels, simultaneously upregulated IL-17 and GLUT1 expression, and partially restored Th17 cell differentiation[5]. VH-298 (50μM) was used to treat HeLa cells and RPE/mRFP-EGFP-SKL cells for 48 hours. VH-298 significantly promoted peroxisomal degradation (pexophagy), increased ABCD3 ubiquitination, and activated HIF-1α[6].

In vivo, VH-298 (30μM; 100μl; every three days) was locally injected into the wound area of hyperglycemic rats for 21 days. VH-298 improved wound healing, activated the HIF-1 signaling pathway, and promoted vascularization in rats[7]. VH-298 (30μM; 100μl; daily) was injected into the reconstructed attachment site area of a Sprague-Dawley rat model with Achilles tendon-calcaneus rupture. VH-298 improved Achilles tendon-calcaneus healing, increased maximum load and failure energy, and activated the HIF signaling pathway in rats[8].

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References:

[1] Frost J, Galdeano C, Soares P, et al. Potent and selective chemical probe of hypoxic signalling downstream of HIF-α hydroxylation via VHL inhibition. Nat Commun. 2016 Nov 4;7:13312.
[2] Ling J, Chen H, Huang M, et al. An mRNA vaccine encoding proteasome-targeted antigen enhances CD8+ T cell immunity. J Control Release. 2025 May 10;381:113578.
[3] Wang Y, Cao Z, Wei Q, et al. VH298-loaded extracellular vesicles released from gelatin methacryloyl hydrogel facilitate diabetic wound healing by HIF-1α-mediated enhancement of angiogenesis. Acta Biomater. 2022 Jul 15;147:342-355.
[4] Qin X, Wu K, Zuo C, et al. The Expression and Role of Hypoxia-induced Factor-1α in Human Tenon's Capsule Fibroblasts under Hypoxia. Curr Eye Res. 2021 Mar;46(3):417-425.
[5] Zhang Q, Wang L, Jiang J, et al. Critical Role of AdipoR1 in Regulating Th17 Cell Differentiation Through Modulation of HIF-1α-Dependent Glycolysis. Front Immunol. 2020 Aug 18;11:2040.
[6] Kim YH, Park NY, Jo DS, et al. Inhibition of VHL by VH298 Accelerates Pexophagy by Activation of HIF-1α in HeLa Cells. Molecules. 2024 Jan 18;29(2):482.
[7] Qiu S, Jia Y, Sun Y, et al. Von Hippel-Lindau (VHL) Protein Antagonist VH298 Improves Wound Healing in Streptozotocin-Induced Hyperglycaemic Rats by Activating Hypoxia-Inducible Factor-(HIF-) 1 Signalling. J Diabetes Res. 2019 Feb 17;2019:1897174.
[8] Qiu S, Jia Y, Tang J, et al. Von Hippel-Lindau (VHL) protein antagonist, VH298, promotes functional activities of tendon-derived stem cells and accelerates healing of entheses in rats by inhibiting ubiquitination of hydroxy-HIF-1α. Biochem Biophys Res Commun. 2018 Nov 10;505(4):1063-1069.

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