VH-298

Cat. No.: HY-100947

CAS No.: 2097381-85-4

Molecular Formula: $C_{27}H_{33}N_5O_4S$

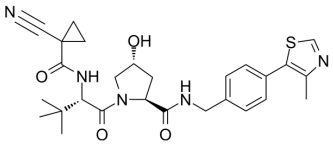
Molecular Weight: 523.65

Target: Ligands for E3 Ligase

Pathway: PROTAC

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 : ≥ 83.3 mg/mL (159.08 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9097 mL	9.5484 mL	19.0967 mL
5 mM	0.3819 mL	1.9097 mL	3.8193 mL
10 mM	0.1910 mL	0.9548 mL	1.9097 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 (4.77 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.77 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

VH-298 is a highly potent inhibitor of the VHL:HIF-α interaction with a K_d value of 80 to 90 nM, used in PROTAC technology.

IC_{50} & Target

Kd: 80 to 90 nM (VHL:HIF-α)[1]

In Vitro

VH-298 is a potent, cell permeable and non-toxic chemical probe that triggers the hypoxic response by blocking the VHL. VH-298 is a highly potent inhibitor of the VHL:HIF-α interaction with K_d values of 90 and 80 nM in isothermal titration

calorimetry and competitive fluorescence polarization assay. VH-298 binds with VHL complex very fast and dissociates slowly. VH-298 at 50 μM concentration exhibits negligible off-target effects in vitro against more than 100 tested cellular kinases, GPCRs and ion channels. VH-298 is cell permeable and not toxic to cells. The measured permeability of VH-298 is found to be 19.4 nm s^{-1}. VH-298 induces concentration- and time-dependent on-target specific accumulation of hydroxylated HIF-α in human cell lines, including HeLa cancer cells and renal cell carcinoma 4 (RCC4) cells. VH-298 increases mRNA levels of EPO by 2.5-fold in RCC4-HA-VHL, but not in VHL-null RCC4-HA, indicating that pharmacological inhibition of VHL is able to stimulate endogenous EPO synthesis. VH-298 proves as effective as hypoxia in raising PHD2 and HK2 protein levels, however in HFF the BNIP3 protein level increases more with VH-298 treatment than hypoxia treatment[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

VH-298 is screened at 50 μM concentration against a panel of 50 kinases. The remaining kinase activity is recorded in the end of the assay. The data is reported as average % activity remaining of assay duplicates for each kinase tested[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [1]

Death of CTLs is analyzed by staining with 4′,6-diamidino-2-phenylindole (DAPI). Cells are plated in 96-well plates at 1×10^6 and treated with VHL inhibitors (VH-298) and respective non-binding cis-analogues for 24 h. Cells are spun down and resuspended in HBSS containing DAPI to identify dead and dying populations[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Discov. 2020 Jun 9;6:35.
- Acta Pharmacol Sin. 2022 Nov 10.
- Curr Opin Chem Biol. 19 October 2021, 100009.
- Hepatol Commun. 2022 Apr 16.
- Bioconjug Chem. 2020 Nov 18;31(11):2564-2575.

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REFERENCES

[1]. Frost J, 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.

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