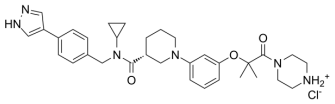
ZW4864

Cat. No.:	HY-132300
CAS No.:	2632259-93-7
Molecular Formula:	$C_{33}H_{43}ClN_6O_3$
Molecular Weight:	607.19
Target:	β-catenin
Pathway:	Stem Cell/Wnt
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 41.67 mg/mL (68.63 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6469 mL	8.2347 mL	16.4693 mL
	5 mM	0.3294 mL	1.6469 mL	3.2939 mL
	10 mM	0.1647 mL	0.8235 mL	1.6469 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: ≥ 2.08 mg/mL (3.43 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ZW4864 is an orally active and selective β catenin/B-Cell lymphoma 9 protein−protein interaction (β catenin/BCL9 PPI) inhibitor. ZW4864 inhibits β catenin/BCL9 PPI with a K_i value of 0.76 μM and an IC_{50} value of 0.87 μM[1].

IC_{50} & Target

IC50: 0.87 μM (β catenin/BCL9 PPI)[1].
Ki: 0.76 μM(β catenin/BCL9 PPI)[1]

In Vitro

ZW4864 (10~40 μM; 24 hours; SW480 and MBA-MD-231 cells) decreases the expression levels of Axin2 and cyclin D1 proteins [1].

ZW4864 (10~40 μM; 72 hours; MDA-MB231, MCF10A and MDA-MB-468 cells) selectively triggeres rapid apoptosis of triple-negative breast cancer cells with hyperactive β-catenin signaling while sparing normal mammary epithelial MCF10A cells[1].

ZW4864 (10~40 μM; 24 hours; SW480 and MBA-MD-231 cells) suppresses the transcription of β-catenin target genes in a

concentration-dependent manner without affecting the expression of HPRT, a house-keeper gene, in both SW480 and Wnt 3a-activated MDA-MB-231 cells[1].

ZW4864 binds with β-catenin and selectively disrupts the protein−protein interaction (PPI) between B-cell lymphoma 9 (BCL9) and β-catenin while sparing the β-catenin/E-cadherin PPI. ZW4864 dose-dependently suppresses β-catenin signaling activation, downregulates oncogenic β-catenin target genes, and abrogates invasiveness of β-catenin-dependent cancer cells. ZW4864 suppresses TOPFlash luciferase activities in β-catenin expressing HEK293 cells in a dose-dependent manner with an IC_{50} of 11 μM. ZW4864 also dose-dependently suppresses the TOPFlash luciferase activities in SW480 and Wnt 3a-activated MDA-MB-468 cells with the IC_{50}s of 7.0 and 6.3 μM, respectively. ZW4864 selectively suppresses transactivation of β-catenin signaling[1].

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

Western Blot Analysis[1]

Cell Line:	SW480 and MBA-MD-231 cells
Concentration:	10~40 μM
Incubation Time:	24 hours
Result:	Decreased the expression levels of Axin2 and cyclin D1 proteins.

Apoptosis Analysis[1]

Cell Line:	MDA-MB231, MCF10A and MDA-MB-468 cells
Concentration:	10~40 μM
Incubation Time:	72 hours
Result:	Selectively triggered rapid apoptosis of triple-negative breast cancer cells with hyperactive β-catenin signaling while sparing normal mammary epithelial MCF10A cells.

RT-PCR[1]

Cell Line:	SW480 and MBA-MD-231 cells
Concentration:	10~40 μM
Incubation Time:	24 hours
Result:	Suppressed the transcription of β-catenin target genes in a concentration-dependent manner without affecting the expression of HPRT, a house-keeper gene, in both SW480 and Wnt 3a-activated MDA-MB-231 cells.

In Vivo

ZW4864 (20 mg/kg; p.o.) exhibits good pharmacokinetic properties with an oral bioavailability (F) of 83 %[1].

ZW4864 (90 mg/kg; p.o.) shows a variation in tumor growth in mice[1].

ZW4864 shows good pharmacokinetic properties and effectively suppresses β-catenin target gene expression in the patient-derived xenograft mouse model[1].

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

Animal Model:	C57BL/6 mice[1]
Dosage:	20 mg/kg (Pharmacokinetic Analysis)
Administration:	P.o.
Result:	Exhibited good pharmacokinetic properties with an oral bioavailability (F) of 83%.

Animal Model:	Mice[1]
Dosage:	90 mg/kg
Administration:	P.o.
Result:	Showed a variation in tumor growth in mice.

REFERENCES

[1]. Wang Z, et al. Discovery of an Orally Bioavailable Small-Molecule Inhibitor for the β-Catenin/B-Cell Lymphoma 9 Protein-Protein Interaction. J Med Chem. 2021;64(16):12109-12131.

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