ZW4864 free base

Cat. No.: HY-132300A

CAS No.: 2632259-92-6

Molecular Formula: $C_{33}H_{42}N_6O_3$

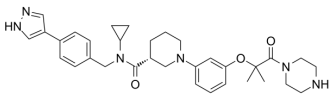
Molecular Weight: 570.72

Target: β-catenin

Pathway: Stem Cell/Wnt

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 : 100 mg/mL (175.22 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7522 mL	8.7609 mL	17.5217 mL
	5 mM	0.3504 mL	1.7522 mL	3.5043 mL
	10 mM	0.1752 mL	0.8761 mL	1.7522 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

ZW4864 (free base) is an orally active and selective β catenin/B-Cell lymphoma 9 protein−protein interaction (β catenin/BCL9 PPI) inhibitor. ZW4864 (free base) 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) (free base) 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) (free base) 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) (free base) 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 (free base) 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 (free base) dose-dependently suppresses β-catenin signaling activation, downregulates oncogenic β-catenin target genes, and abrogates invasiveness of β-catenin-dependent cancer cells. ZW4864 (free base) suppresses TOPFlash luciferase activities in β-catenin expressing HEK293 cells in a dose-dependent manner with an IC_{50} of 11 μM. ZW4864 (free base) 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 (free base) 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.) (free base) exhibits good pharmacokinetic properties with an oral bioavailability (F) of 83 %[1].
ZW4864 (90 mg/kg; p.o.) (free base) shows a variation in tumor growth in mice[1].
ZW4864 (free base) 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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