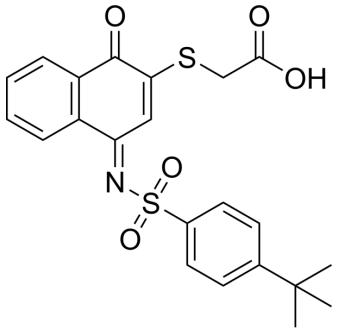
KPT-6566

Cat. No.:	HY-123847
CAS No.:	881487-77-0
Molecular Formula:	$C_{22}H_{21}NO_5S_2$
Molecular Weight:	443.54
Target:	PIN1
Pathway:	PI3K/Akt/mTOR
Storage:	4°C, protect from light, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 19.23 mg/mL (43.36 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2546 mL	11.2729 mL	22.5459 mL
	5 mM	0.4509 mL	2.2546 mL	4.5092 mL
	10 mM	0.2255 mL	1.1273 mL	2.2546 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: 1.92 mg/mL (4.33 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1 mg/mL (2.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KPT-6566 is a selective and covalent prolyl isomerase PIN1 inhibitor, covalently binds to the catalytic site of PIN1, selectively inhibits and degrades PIN1. KPT-6566 shows an IC_{50} value of 640 nM and a K_i value of 625.2 nM for PIN1 PPIase domain. KPT-6566 can be used for the research of cancer[1].

IC_{50} & Target

IC50: 640 nM (PIN1 PPIase)[1]
Ki: 625.2 nM (PIN1 PPIase)[1]

In Vitro

KPT-6566 (1-5 μM; 0-8 d) inhibits WT fibroblasts proliferation[1].
KPT-6566 (0-10 μM; 48 h) inhibits normal breast epithelial cells and cancer cells viability via a PIN1-dependent manner[1].
KPT-6566 (0-10 μM; 48 h) affects hyperphosphorylated pRB level, Cyclin D1 and PIN1 concentration[1].
KPT-6566 (2.5-5 μM; 48 h) inhibits the mut-p53, NOTCH1 and NRF2 pathways[1].

KPT-6566 (0-5 μM; 48 h) induces DNA damage via a PIN1-dependent way[1].

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

Cell Proliferation Assay[1]

Cell Line:	Immortalized fibroblasts derived from WT and Pin1 KO mouse embryos
Concentration:	1 and 5 μM
Incubation Time:	0-8 days
Result:	Dose-dependently inhibited proliferation of WT fibroblasts, while showed no effect on Pin1 KO fibroblasts.

Cell Viability Assay[1]

Cell Line:	MCF10A, HMEC, HeLa, LNCaP, SKOV-3, PANC-1, PC-3, MDA-MB-468 and MDA-MB-231 cells
Concentration:	0-10 μM
Incubation Time:	48 hours
Result:	Inhibited normal breast epithelial cells and cancer cells viability even at a low concentration and increased the concentration of PIN1 in MDA-MB-468, SKOV-3, PC-3, LNCaP and PANC-1.

Western Blot Analysis[1]

Cell Line:	Immortalized fibroblasts derived from WT and Pin1 KO mouse embryos and PIN1 KO MDA-MB-231 cells
Concentration:	0-10 μM
Incubation Time:	48 hours
Result:	Decreased hyperphosphorylated pRB and Cyclin D1 levels, dose- and time-dependently promoted degradation of PIN1 .

Western Blot Analysis[1]

Cell Line:	MDA-MB-231, MCF10A, MDA-MB-468 and MDA-MB-231 cells
Concentration:	0, 2.5 and 5 μM
Incubation Time:	48 hours
Result:	Dose-dependently increased H2AX phosphorylation and caused H2AX phosphorylation in MCF10A, MDA-MB-468 and MDA-MB-231 cell lines. Increased H2AX phosphorylation while other inhibitors such as ATRA, PiB and Juglone disabled to induce H2AX phosphorylation at same concentration. Achieved DNA damage through formation of DNA adducts.

RT-PCR[1]

Cell Line:	MDA-MB-231 cells
Concentration:	2.5 and 5 μM
Incubation Time:	48 hours
Result:	Dose-dependently inhibitd the activation of mut-p53 and NOTCH1 pathways which are

	controlled by PIN1. Inhibitd the expression of cFOS HO1, NQO1, TXNRD1 and DNAJAB, and induced cellular responses to oxidative stress.

In Vivo

KPT-6566 (5 mg/kg; i.p. once a day for 26 days) shows no toxicity to mice[1].

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Animal Model:	6-week-old female mice with 1 million of MDA-MB-231Luc^6 cells injection[1]
Dosage:	5 mg/kg
Administration:	Intraperitoneal injection; 5 mg/kg once a day; for 26 days
Result:	Exibited no sign of local or systemic and organ toxicity by post mortem morphologic analyses.

REFERENCES

[1]. Campaner E, et al. A covalent PIN1 inhibitor selectively targets cancer cells by a dual mechanism of action. Nat Commun. 2017 Jun 9;8:15772.

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