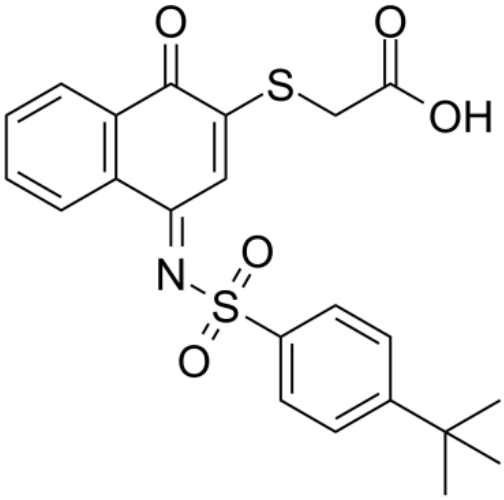
Product Data Sheet

Product Name: KPT-6566
Cat. No.: GC38577

Chemical Properties

Cas. No.	881487-77-0		
SMILES	O=C(O)CSC(C1=O)=C/C(C2=C1C=CC=C2)=N\S(=O)(C3=CC=C(C(C)(C)C)C=C3)=O		
Formula	$C_{22}H_{21}NO_5S_2$	M.Wt	443.54
Solubility	DMSO : 19.23 mg/mL (43.36 mM; Need ultrasonic)	Storage	4°C, protect from light, stored under nitrogen
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]:

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Cell lines	Immortalized mouse pancreatic stellate cells (immortalized mouse PSCs)
Preparation Method	Immortalized mouse PSCs were grown in DMEM supplemented with 10% FBS at 37°C, 5% CO_2. PSCs were pretreated with KPT-6566 (10μM) for 48h, followed by TGF-β (5ng/ml) stimulation.
Reaction Conditions	10μM; 48h pretreatment
Applications	KPT-6566 reduced TGF-β-driven upregulation of aSMA and PALLD protein in immortalized mouse PSCs.

Animal experiment [2]:

Animal models	Female BALB/c nude mice (4 weeks old)
Preparation Method	3×10^6 KHM5M cells resuspended in Matrigel were subcutaneously injected into the flank region of mice to establish subcutaneous xenograft models. When tumor volume reached 50-100mm^3, mice were intraperitoneally administered with KPT-6566 (20mg/kg) or vehicle control, three times per week for 21 days. Tumors and major organs (heart, liver, spleen, lung, kidney) were collected at the experimental endpoint for subsequent analysis.
Dosage form	20mg/kg; i.p.; three times per week for 21 days
Applications	KPT-6566 suppressed xenograft tumor growth, with reduced tumor volume and weight, upregulated NCOA4 expression, reduced FTH1 levels and Ki67 staining in tumor tissues, and no obvious histopathological abnormalities were detected in heart, liver, spleen, lung and kidney.

Caution: Product has not been fully validated for medical applications. For research use only.
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References:
[1] Bowman CL, Daniel CJ, Carlson EJ, et al. The Prolyl Isomerase PIN1 Impacts Fibroblast Differentiation States and Crosstalk in Pancreatic Cancer. Cancer Res. 2025 Dec 15;85(24):4899-4917.
[2] Sun Z, Bai F, Liang M, et al. Pin1 targets phosphorylated NCOA4 for K29/K48-linked ubiquitination to suppress ferritinophagy and ferroptosis in anaplastic thyroid cancer. Cell Death Dis. 2026 Jul 1.

Background

KPT-6566 is a selective, covalent PIN1 (peptidyl-prolyl cis-trans isomerase) inhibitor (IC_{50}=640nM; K_i=625.2nM). KPT-6566 covalently binds to the catalytic site of PIN1 to selectively inhibit and degrade PIN1. KPT-6566 induces ROS release and DNA damage to activate apoptosis. KPT-6566 can be used for research on colorectal cancer and other cancers[1-4].

In vitro, KPT-6566 (0-10μM) treated HeLa and SiHa cervical cancer cells for 24h. KPT-6566 inhibited cell proliferation and colony formation and induced apoptosis. KPT-6566 enhanced the killing effect of cisplatin (DDP) on cells[5]. KPT-6566 (10μM) pretreated immortalized mouse pancreatic stellate cells for 48h, followed by TGF-β (5ng/ml) stimulation for 24h. KPT-6566 inhibited TGF-β-driven myofibroblast (myCAF) activation and downregulated aSMA and PALLD protein expression[6].

In vivo, KPT-6566 (5mg/kg; once daily) was intraperitoneally injected into MDA-MB-231 tail vein lung colonization model nude mice for 26 consecutive days. KPT-6566 significantly inhibited lung metastasis growth without obvious systemic or organ toxicity[7]. KPT-6566 (20mg/kg; every 3 days) was intraperitoneally injected into KHM5M subcutaneous xenograft BALB/c nude mice (dosing started when tumor volume reached 50-100mm^3) for 21 consecutive days. KPT-6566 significantly inhibited xenograft tumor volume and weight, upregulated intratumoral NCOA4, and downregulated FTH1 and Ki67[8].

References:
[1] Wu Y, Guo J, Zhang Y, et al. Targeting PIN1 in Pancreatic Tumor Microenvironment with Peptide Amphiphiles Unleashes Immune Checkpoint Therapy. Adv Healthc Mater. 2026 Jan;15(3):e03114.
[2] Zhu Q, Chen X, Lin Z. Discovery of KPT-6566 as STAG1/2 Inhibitor sensitizing PARP and NHEJ

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Inhibitors to suppress tumor cells growth in vitro. DNA Repair (Amst). 2024 Dec;144:103784.
[3] Ozleyen A, Duran GN, Donmez S, et al. Identification and inhibition of PIN1-NRF2 protein-protein interactions through computational and biophysical approaches. Sci Rep. 2025 Mar 14;15(1):8907.
[4] Zhang Z, Hu Q, Ye S, et al. Inhibition of the PIN1-NRF2/GPX4 axis imparts sensitivity to cisplatin in cervical cancer cells. Acta Biochim Biophys Sin (Shanghai). 2022 Aug 25;54(9):1325-1335.
[5] Guo YT, Lu Y, Jia YY, et al. Predictive Value of Pin1 in Cervical Low-Grade Squamous Intraepithelial Lesions and Inhibition of Pin1 Exerts Potent Anticancer Activity against Human Cervical Cancer. Aging Dis. 2020 Feb;11(1):44-59.
[6] Bowman CL, Daniel CJ, Carlson EJ, et al. The Prolyl Isomerase PIN1 Impacts Fibroblast Differentiation States and Crosstalk in Pancreatic Cancer. Cancer Res. 2025 Dec 15;85(24):4899-4917.
[7] Campaner E, Rustighi A, Zannini A, et al. A covalent PIN1 inhibitor selectively targets cancer cells by a dual mechanism of action. Nat Commun. 2017 Jun 9;8:15772.
[8] Sun Z, Bai F, Liang M, et al. Pin1 targets phosphorylated NCOA4 for K29/K48-linked ubiquitination to suppress ferritinophagy and ferroptosis in anaplastic thyroid cancer. Cell Death Dis. 2026 Jul 1.

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