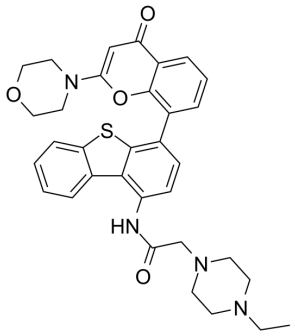
KU-0060648

Cat. No.:	HY-13431
CAS No.:	881375-00-4
Molecular Formula:	$C_{33}H_{34}N_4O_4S$
Molecular Weight:	582.71
Target:	DNA-PK; PI3K; mTOR
Pathway:	Cell Cycle/DNA Damage; PI3K/Akt/mTOR
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 : 2.78 mg/mL (4.77 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7161 mL	8.5806 mL	17.1612 mL
	5 mM	---	---	---
	10 mM	---	---	---

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: ≥ 0.28 mg/mL (0.48 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.28 mg/mL (0.48 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.28 mg/mL (0.48 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KU-0060648 is a dual inhibitor of PI3K and DNA-PK with IC_{50}s of 4 nM, 0.5 nM, 0.1 nM, 0.594 nM and 8.6 nM for PI3Kα, PI3Kβ, PI3Kγ, PI3Kδ and DNA-PK, respectively[1].

IC_{50} & Target

PI3Kα	PI3Kβ	PI3Kγ	PI3Kδ
4 nM (IC_{50})	0.5 nM (IC_{50})	0.594 μM (IC_{50})	0.1 nM (IC_{50})

DNA-PK
8.6 nM (IC_{50})

In Vitro

KU-0060648 inhibits cellular DNA-PK auto-phosphorylation with IC_{50} values of 0.019 μM (MCF7 cells) and 0.17 μM (SW620 cells), and PI-3K-mediated AKT phosphorylation with IC_{50} values of 0.039 μM (MCF7 cells) and >10 μM (SW620 cells)[1].
KU-0060648 (30-500 nM; 72 hours) dose-dependently inhibits HepG2 cell proliferation, IC_{50}=134.32nM[2].
KU-0060648 (0.1-1 μM□5 days) inhibits cell lines growth with GI_{50}s of 0.95 μM, 0.21 μM, 0.27 μM, 0.41 μM and 1 μM in SW620, LoVo, MCF7, T47D and MDA-MB-231 cells[1].
KU-0060648 (100-300 nM;12 hours) significantly inhibits activation of PI3K (p85 phosphorylation), AKT (Ser-473 and Thr-308 phosphorylations) and mTOR (p70S6K1 Thr-389 phosphorylation) in HepG2/Huh-7 lines and primary human HCC cells[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	Human breast (MCF7, T47D and MDA-MB-231) and colon (LoVo and SW620) cancer cells
Concentration:	0.1-1 μM
Incubation Time:	5 days
Result:	Resulted in> 50% inhibition of cell growth in all cell lines.

Western Blot Analysis[2]

Cell Line:	HCC cells; HepG2/Huh-7 cells
Concentration:	100-300 nM
Incubation Time:	12 hours
Result:	Inhibited phosphatidylinositol 3-kinase (PI3K) and in-activates AKT-mTOR signaling.

In Vivo

KU-0060648 (intraperitoneal injection; 10 and 50 mg/kg; once daily; daily for 21 days) dramatically inhibits HepG2 xenograft growth in nude mice, the tumor weights (at week 5) of KU-0060648 group mice are dramatically lighter than that of vehicle control mice and exert a dose-dependent effect in vivo[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	HepG2 xenograft nude mice model[1]
Dosage:	10 and 50 mg/kg
Administration:	Intraperitoneal injection; 10 and 50 mg/kg; once daily; daily for 21 days
Result:	Suppressed HepG2 xenograft growth in nude mice.

CUSTOMER VALIDATION

- Nat Methods. 2024 Feb 1.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Munck JM, et al. Chemosensitization of cancer cells by KU-0060648, a dual inhibitor of DNA-PK and PI-3K. Mol Cancer Ther. 2012 Aug;11(8):1789-98.

[2]. Chen MB, et al. KU-0060648 inhibits hepatocellular carcinoma cells through DNA-PKcs-dependent and DNA-PKcs-independent mechanisms. Oncotarget. 2016 Mar

29;7(13):17047-59.

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