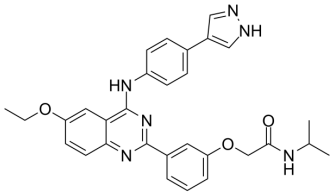
KL-11743

Cat. No.:	HY-145597
CAS No.:	1369452-53-8
Molecular Formula:	$C_{30}H_{30}N_6O_3$
Molecular Weight:	522.6
Target:	GLUT
Pathway:	Membrane Transporter/Ion Channel
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 : 25 mg/mL (47.84 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9135 mL	9.5675 mL	19.1351 mL
	5 mM	0.3827 mL	1.9135 mL	3.8270 mL
	10 mM	0.1914 mL	0.9568 mL	1.9135 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.98 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KL-11743 is a potent, orally active, and glucose-competitive inhibitor of the class I glucose transporters, with IC_{50}s of 115, 137, 90, and 68 nM for GLUT1, GLUT2, GLUT3, and GLUT4, respectively. KL-11743 specifically blocks glucose metabolism. KL-11743 can synergize with electron transport inhibitors to induce cell death[1][2][3].

IC_{50} & Target

GLUT1	GLUT2	GLUT3	GLUT4
115 nM (IC_{50})	137 nM (IC_{50})	90 nM (IC_{50})	68 nM (IC_{50})

In Vitro

KL-11743 (compound 8) competes with glucose for binding to GLUT1, with IC_{50}s of 33 nM and 268 nM at 0.37 mM and 10 mM glucose, respectively[1].

KL-11743 (39-10000 nM; 24-72 h) dose-dependently inhibits the growth of HT-1080 cells, with an IC_{50} of 677 nM[3].

KL-11743 inhibits the growth of KEAP1-mutant lung cancer cells with more potency compared to KEAP1-WT lung cancer cells [4].

KL-11743 (0.001-10 μM) induces a rapid increase in the phosphorylation of AMPK and acetyl-coenzyme A carboxylase in HT-1080 cells [3].
KL-11743 (2 μM) inhibits glucose uptake in 786-O cells. KL-11743 increases NADP+/NADPH in NCl-H226 cells. KL-11743 induces cell death in SLC7A11-high cancer cell lines (NCl-H226 and UMRC6 cells)[2].
KL-11743 (0.001-10 μM) inhibits both glucose consumption, lactate secretion, and 2DG transport in HT-1080 fibrosarcoma cells, with IC_{50}s of 228, 234, and 87 nM, respectively, and fully inhibited glycolytic ATP production in oligomycin-treated cells with an IC_{50} of 127 nM[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[3]

Cell Line:	HT-1080 cells
Concentration:	39, 78, 156, 312, 625, 1250, 2500, 5000, 10000 nM
Incubation Time:	24, 48, 72 hours
Result:	Inhibited the growth of HT-1080 cells in a dose-dependent manner.

In Vivo

KL-11743 (100 mg/kg; i.p. every two days for 5 weeks) decreases the growth of SLC7A11-high NCI-H226 xenograft tumors and was well-tolerated in vivo[2].
KL-11743 (30-100 mg/kg; a single p.o.) significantly elevates blood glucose levels and delays glucose clearance in mice challenged with 5 g/kg glucose[3].
KL-11743 significantly suppresses the growth of KEAP1 KO tumors[4].
Plasma levels of KL-11743 (100 mg/kg; i.p.) are maintained at inhibitory levels for most of the 24-hour dosing period[2].
KL-11743 (p.o) exhibits moderate oral between 30% and 15%, and favorable and dose-linear plasma exposure profile reaching concentrations of approximately 20 μM in mice (10-100 mg/kg) and rats (10-300 mg/kg)[3].
KL-11743 exhibits comparable half-lives ranging between 2.04 and 5.38 h in rats (10 mg/kg for i.v.; 10-300 mg/kg for p.o.), and 1.45-4.75 h in mice (10 mg/kg for i.v. and i.p.; 10-100 mg/kg for p.o.)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	4 to 6-week-old athymic nude mice (Foxn1nu/Foxn1nu) were injected with NCI-H226 cells100 mg/kg[2]
Dosage:	100 mg/kg
Administration:	I.p. every two days for 5 weeks
Result:	Inhibited the growth of tumors. Exhibited extensive necrotic cell death. Decreased PPP intermediate 6-phosphogluconate levels and increased NADP+/NADPH ratio.

REFERENCES

[1]. Liu KG, et, al. Discovery and Optimization of Glucose Uptake Inhibitors. J Med Chem. 2020 May 28;63(10):5201-5211.

[2]. Liu X, et, al. Cystine transporter regulation of pentose phosphate pathway dependency and disulfide stress exposes a targetable metabolic vulnerability in cancer. Nat Cell Biol. 2020 Apr;22(4):476-486.

[3]. Olszewski K, et, al. Inhibition of glucose transport synergizes with chemical or genetic disruption of mitochondrial metabolism and suppresses TCA cycle-deficient tumors. Cell Chem Biol. 2021 Oct 22;S2451-9456(21)00441-4.

[4]. Koppula P, et, al. KEAP1 deficiency drives glucose dependency and sensitizes lung cancer cells and tumors to GLUT inhibition. iScience. 2021 May 25;24(6):102649.

Caution: Product has not been fully validated for medical applications. For research use only.

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