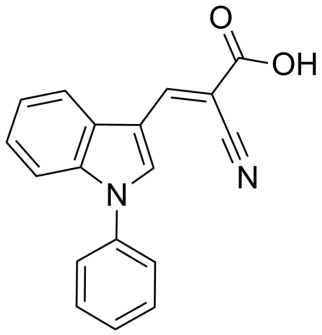
UK-5099

Cat. No.:	HY-15475
CAS No.:	56396-35-1
Molecular Formula:	$C_{18}H_{12}N_2O_2$
Molecular Weight:	288.3
Target:	Mitochondrial Metabolism
Pathway:	Metabolic Enzyme/Protease
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 : ≥ 50 mg/mL (173.43 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.4686 mL	17.3430 mL	34.6861 mL
	5 mM	0.6937 mL	3.4686 mL	6.9372 mL
	10 mM	0.3469 mL	1.7343 mL	3.4686 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: ≥ 2.5 mg/mL (8.67 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.67 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UK-5099 (PF-1005023) is a potent inhibitor of the mitochondrial pyruvate carrier (MPC). UK-5099 (PF-1005023) inhibits pyruvate-dependent O_2 consumption with an IC_{50} of 50 nM.

IC_{50} & Target

IC50: 50 nM (MPC)[1]

In Vitro

The trypanosomal pyruvate carrier is found to be rather insensitive to inhibition by alpha-cyano-4-hydroxycinnamate (K_i=17 mM) but can be completely blocked by UK-5099 (K_i=49 microM)[2]. UK-5099 also inhibits the monocarboxylate transporter (MCT) [3]. UK5099 significantly inhibits the glucose-stimulated rise in oxygen consumption in a dose-dependent manner and at 150 μM reduced oxygen consumption below basal levels. UK5099 reduces ATP levels and increases ADP and AMP levels in

	832/13 cells[4]. The UK5099 treated cells show significantly higher proportion of side population fraction and express higher levels of stemness markers Oct3/4 and Nanog. UK5099 application may be an ideal model for Warburg effect studies[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The MPC inhibitor UK5099 increases the glucose excursion seen during an intraperitoneal glucose tolerance test in C57BLK mice[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [4]	The 832/13 cell line is used for experiments. Cell viability is measured using CellTiter Blue. The assay is based on cellular reduction of resazurin to resorufin. Appearance of resorufin is monitored by fluorescence emission at 585 nm using a Spectramax M5 microplate reader with excitation at 555 nm. For UK5099-treated cells, cells are allowed to recover for 1 h before measuring cell viability. Data are expressed as -fold relative to no treatment or siCtrl[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	C57BLK mice are fasted for 16 h prior to glucose challenge. UK5099 (32 μmol/kg of body weight) or DMSO in PBS is injected into the intraperitoneal cavity 30 min before injecting glucose (1.5 mg of glucose/g of body weight). Blood glucose levels are measured at 0, 10, 20, 30, 60, and 120 min after glucose injection[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Immunol. 2023 Mar;24(3):423-438.
- Cell Metab. 2022 Sep 7;S1550-4131(22)00359-X.
- Nat Commun. 2023 Jul 14;14(1):4129.
- Theranostics. 2020 May 16;10(14):6483-6499.
- Redox Biol. 2024 Mar 4:71:103112.

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REFERENCES

[1]. Halestrap AP. The mitochondrial pyruvate carrier. Kinetics and specificity for substrates and inhibitors. Biochem J. 1975 April; 148(1): 85-96.

[2]. Wiemer EA, et al. The inhibition of pyruvate transport across the plasma membrane of the bloodstream form of Trypanosoma brucei and its metabolic implications. Biochem J. 1995 Dec 1;312 (Pt 2):479-84.

[3]. Hinoi E, et al. A molecular mechanism of pyruvate protection against cytotoxicity of reactive oxygen species in osteoblasts. Mol Pharmacol. 2006 Sep;70(3):925-35. Epub 2006 Jun 9.

[4]. Patterson JN, et al. Mitochondrial metabolism of pyruvate is essential for regulating glucose-stimulated secretion. J Biol Chem. 2014 May 9;289(19):13335-46.

[5]. Zhong Y, et al. Application of mitochondrial pyruvate carrier blocker UK5099 creates metabolic reprogram and greater stem-like properties in LnCap prostate cancer cells in vitro. Oncotarget. 2015 Nov 10;6(35):37758-69.

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

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