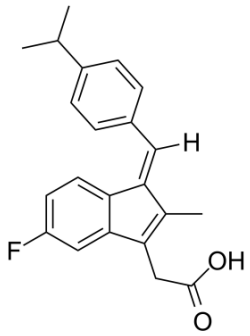
K-80003

Cat. No.:	HY-U00458
CAS No.:	1292821-90-9
Molecular Formula:	$C_{22}H_{21}FO_2$
Molecular Weight:	336.4
Target:	Akt
Pathway:	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 : 30 mg/mL (89.18 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.9727 mL	14.8633 mL	29.7265 mL
	5 mM	0.5945 mL	2.9727 mL	5.9453 mL
	10 mM	0.2973 mL	1.4863 mL	2.9727 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: ≥ 3 mg/mL (8.92 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

K-80003 is a potent inhibitor of tRXRα-dependent Akt activation and cancer cell growth.

IC_{50} & Target

Akt

In Vitro

When MCF-7 cells are cotreated with K-80003, TNFα-induced colocalization of tRXRα with p85α in the cytoplasm is inhibited, resulting in tRXRα nuclear localization. Western blotting shows that K-80003-stabilized tetrameric form of tRXRα is found exclusively in the nuclear fraction, while tRXRα monomer is distributed both in the nuclear and cytoplasmic fractions[2].

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

In Vivo

K-80003 is a potent inhibitor of AKT activation by all-trans-retinoic acid. K-80003 displays enhanced efficacy in inhibiting tRXRα-dependent AKT activation and tRXRα tumor growth in animals. K-80003 has high affinity to RXRα but lacks COX inhibitory activity[1].

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PROTOCOL

Cell Assay [2]

MCF-7 cells cotransfected with Myc-RXRα, Myc-tRXRα, tRXRα/L433D and p85α are pretreated with or without K-80003 (5 μM) for 3 h before exposed to TNFα (10 ng/mL) for 30 min. Cells are immunostained with anti-Myc and anti-p85α antibody, and their subcellular localization revealed by confocal microscopy. HEK293T cells cotransfected with Myc-tRXRα are treated with or without K-80003 (5 μM) for 6 h. Nuclear (N) and cytoplasmic (C) fractions are prepared, subjected to BS3 crosslinking, and analysed by western blotting using anti-Myc antibody. The purity of fractions is examined by analysing the expression of nuclear PARP and cytoplasmic α-tubulin in non-crosslinked fractions. One of three similar experiments is shown[2].

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Animal Administration [1]

Mice[1]

Nude mice (BALB/c, 4-5-week old) are injected subcutaneously with 100 μL of cells (2×10^6). For drug treatment, mice (n=6) are treated intraperitoneally after 7 days of transplantation with Corn oil, Sulindac (60 mg/kg), or K-80003 (60 mg/kg) once every other day (six injections). Body weight and tumor sizes are measured every 4 days.

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

REFERENCES

[1]. Zhou H, et al. NSAID sulindac and its analog bind RXRalpha and inhibit RXRalpha-dependent AKT signaling. Cancer Cell. 2010 Jun 15;17(6):560-73.

[2]. Chen L, et al. Modulation of nongenomic activation of PI3K signalling by tetramerization of N-terminally-cleaved RXRα. Nat Commun. 2017 Jul 17;8:16066.

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