# TK-129

**Cat. No.:** HY-151483

**Molecular Formula:** $C_{15}H_{23}N_5O_2$

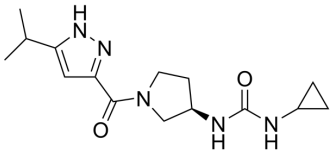
**Molecular Weight:** 305.38

**Target:** Histone Demethylase

**Pathway:** Epigenetics

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| In solvent | -80°C | 6 months |
| | -20°C | 1 month |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 100 mg/mL (327.46 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 3.2746 mL | 16.3730 mL | 32.7461 mL |
| | 5 mM | 0.6549 mL | 3.2746 mL | 6.5492 mL |
| | 10 mM | 0.3275 mL | 1.6373 mL | 3.2746 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 (8.19 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.19 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.19 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

TK-129 is an orally active, low-toxicity, potent KDM5B inhibitor (with high affinity; $IC_{50}$=44 nM). TK-129 exerts cardioprotective effects by inhibiting KDM5B and blocking the KDM5B-associated Wnt pathway. TK-129 reduces ang II-induced activation of cardiac fibroblasts in vitro and reduces isoprenaline-induced myocardial remodelling and fibrosis in vivo. TK-129 can be used in studies of cardiovascular disease[1].

**$IC_{50}$ & Target**

KDM5
44 nM ($IC_{50}$)

**In Vitro**

TK-129 mediates inhibition of KDM5B activity significantly reduces the activation, migration, and proliferation of

myofibroblasts induced by Ang II in vitro[1].
TK-129 (10 μM; 48 h) shows low cytotoxicity in NRCFs and NRCMs[1].
TK-129 (0.1, 0.2, 0.3, 0.4, 0.5 μM; 48 h) can engage toand inhibit KDM5B activity in NRCFs[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Cytotoxicity Assay[1]

| | |
|---|---|
| Cell Line: | NRCFs and NRCMs |
| Concentration: | 10 μM |
| Incubation Time: | 48 h |
| Result: | Exhibited the cell survival rates were almost more than 90%. |

Western Blot Analysis[1]

| | |
|---|---|
| Cell Line: | NRCFs |
| Concentration: | 0.1, 0.2, 0.3, 0.4, 0.5 μM |
| Incubation Time: | 48 h |
| Result: | Increased the expression level of KDM5B substrate H3K4me3 protein in a concentration-dependent manner. |

**In Vivo**

TK-129 (2 g/kg; p.o.; single) shows good bio-safety in mice[1].
TK-129 (50 mg/kg; p.o.; twice daily for 24 days) effectively reduces isoproterenol-induced pathological myocardial remodeling in vivo[1].
TK-129 (2 or 10 mg/kg; i.v. or p.o.; single) demonstrates favorable PK properties in vivo[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|---|---|
| Animal Model: | Wild C57BL/6 mice (8 to 10-week-old; half male and half female)[1]. |
| Dosage: | 2 g/kg |
| Administration: | Oral gavage, single. |
| Result: | Exhibited all mice in the acute toxicity group survived and gained weight normally, after 2 weeks. |

| | |
|---|---|
| Animal Model: | C57BL/6 mice (isoproterenol (ISO)-induced)[1]. |
| Dosage: | 50 mg/kg |
| Administration: | Oral gavage, twice daily for 24 days. |
| Result: | Alleviated myocardial remodeling induced by ISO in vivo. |

| | |
|---|---|
| Animal Model: | Male SD Rats (223.5-265.1 g)[1]. |
| Dosage: | 2 mg/kg (for i.v.); 10 mg/kg (for p.o.). |
| Administration: | Intravenous injection or oral gavage; single. |
| Result: | Pharmacokinetic Parameters of TK-129 in Male SD Rats[1]. |

| | PO (10 mg/kg) | IV (2 mg/kg) |
|---|---|---|
| CL (L/h/kg) | 9.9 | 4.2 |
| $V_{ss}$ (L/kg) | 33.4 | 2.7 |
| $T_{1/2}$ (h) | 2.4 | 0.4 |
| $T_{max}$ (h) | 0.4 | - |
| $C_{max}$ (ng/mL) | 709.7 | 1229.1 |
| $AUC_{0-24}$ (ng/mL•h) | 1038.2 | 479.6 |
| F (%) | 42.37 | - |

## REFERENCES

[1]. Tang K, et al. Discovery of Novel Pyrazole-Based KDM5B Inhibitor TK-129 and Its Protective Effects on Myocardial Remodeling and Fibrosis. J Med Chem. 2022 Sep 16.



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