Setanaxib

Cat. No.: HY-12298

CAS No.: 1218942-37-0

Molecular Formula: $C_{21}H_{19}ClN_4O_2$

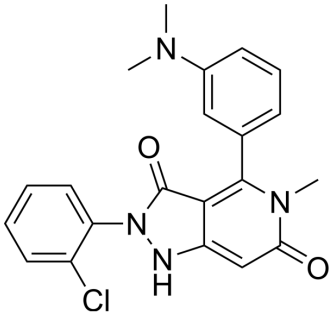
Molecular Weight: 394.85

Target: NADPH Oxidase; Ferroptosis

Pathway: Metabolic Enzyme/Protease; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (316.58 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5326 mL	12.6630 mL	25.3261 mL
5 mM	0.5065 mL	2.5326 mL	5.0652 mL
10 mM	0.2533 mL	1.2663 mL	2.5326 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (6.33 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.33 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.43 mg/mL (3.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Setanaxib (GKT137831) is a selective NADPH oxidase (NOX1/4) inhibitor with K_is of 140 and 110 nM, respectively.

IC_{50} & Target

NOX1	NOX4

In Vitro

Setanaxib (GKT137831) is a potent Nox1/4 inhibitor (K_is=140±40/110±30 nM)[1]. Administration of Setanaxib (GKT137831) throughout the 72-hour period of normoxia or hypoxia exposure attenuates HPASMC proliferation under normoxic conditions at the 20 μM concentration but had no effect on proliferation in normoxic HPAECs. In the prevention paradigm,

	Setanaxib (GKT137831) attenuates hypoxia-induced HPASMC and HPAEC proliferation at 5 and 20 μM. Complementary assays of cell proliferation measuring the expression of PCNA or manual cell counting confirmed that Setanaxib (GKT137831) attenuates hypoxia-induced pulmonary vascular cell proliferation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	During the last half of CCl_4 injections, some mice are treated with Setanaxib (GKT137831) daily. CCl_4-induced liver fibrosis is more pronounced in SOD1mu compared to WT mice. Liver fibrosis in both SOD1mu and WT mice is attenuated by Setanaxib (GKT137831) treatment. The increased hepatic α-SMA expression is markedly decreased in SOD1mu mice treated with Setanaxib (GKT137831), to a level similar to that of WT mice given the NOX1/4 inhibitor[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Monolayers of HPAECs and HPASMCs are propagated in culture and placed in normoxic (21% O_2, 5% CO_2) or hypoxic (1% O_2, 5% CO_2) conditions for 72 hours. Setanaxib (GKT137831) (0.1-20 μM), or vehicle (1% DMSO) are added to the culture medium at the onset (prevention regimen) or during the last 24 hours (intervention regimen) of a 72-hour hypoxia exposure regimen [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Specific pathogen-free, wild-type (WT) C57BL/6J mice are used. For the carbon tetrachloride (CCl_4) model of liver fibrosis, 6 week old male mice are injected intraperitoneally with CCl_4, which is diluted 1:3 in corn oil, or with vehicle (corn oil) at a dose of 0.5 μL/g of body weight twice a week for a total of 12 injections. During the last half of CCl_4 treatment, mice are treated with 60 mg/kg of the NOX1/4 inhibitor Setanaxib (GKT137831) or vehicle by intragastric injection daily. Mice are sacrificed 48 hours after the last CCl_4 injection. For the bile duct ligation (BDL) model, 6 week old male mice are anesthetized. After laparotomy, the common bile duct is ligated twice and the abdomen closed. The sham operation is performed similarly without BDL. From 11 days after operation, mice are treated with 60 mg/kg of the NOX1/4 inhibitor Setanaxib (GKT137831) or vehicle by daily intragastric lavage. Mice are sacrificed 21 days after operation. Serum levels of alanine aminotransferase (ALT) are measured with a commercial kit. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2024 Jul;631(8021):654-662.
- Signal Transduct Target Ther. 2024 Mar 4;9(1):58.
- Redox Biol. 2023 Apr 20, 102702.
- Redox Biol. 2022: 102587.
- Mol Syst Biol. 2021 Oct;17(10):e10480.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Aoyama T, et al. Nicotinamide adenine dinucleotide phosphate oxidase in experimental liver fibrosis: GKT137831 as a novel potential therapeutic agent. Hepatology. 2012 Dec;56(6):2316-27.

[2]. Green DE, et al. The Nox4 inhibitor GKT137831 attenuates hypoxia-induced pulmonary vascular cell proliferation. Am J Respir Cell Mol Biol. 2012 Nov;47(5):718-26.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA