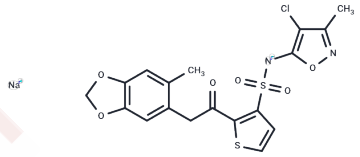
Data Sheet (Cat.No.T6672)

TargetMol

Sitaxsentan sodium

Chemical Properties



CAS No. : 210421-74-2

Formula: C18H14ClN2O6S2·Na

Molecular Weight: 476.89

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Sitaxsentan sodium (TBC11251 sodium salt) is a highly selective antagonist of endothelin A receptors.
Targets(IC50)	Endothelin Receptor
In vitro	Sitaxsentan (administered at 5 mg/kg 10 minutes before hypoxic onset) completely inhibits hypoxia-induced vasoconstriction, with no significant difference observed compared to the control group exposed to air. Oral administration of Sitaxsentan significantly attenuates the increase in mean pulmonary arterial pressure (MPAP), whereas its application in rats exposed to normal oxygen levels does not affect MPAP. Moreover, the use of Sitaxsentan alone can restrict the increase in thickness of the media (MT) caused by shunting.
In vivo	Sitaxsentan and Bosentan, at higher concentrations, attenuate NTCP transport and inhibit human liver transport proteins, offering a potential mechanism for the increased hepatotoxicity observed in these drugs in a clinical setting. Sitaxsentan, alone or in combination with sildenafil, can completely prevent the upregulation of endothelin-1 and ETB receptor expressions. The use of Sitaxsentan alone partially restores the expression of BMPR-1A and BMPR-2. Co-administration with sildenafil further restores the expression of BMPR-1A and BMPR-2, although levels remain reduced compared to the control.
Kinase Assay	Ligand binding studies: Binding studies are performed in a 30 mM HEPES buffer, pH 7.4, containing 150 mM NaCl, 5 mM MgCl2, and 0.05% bacitracin using 2 mg/tube (ETA) or 0.75 mg/tube (ETB) membrane. Sitaxentan sodium is dissolved in DMSO and diluted with the assay buffer to give a final concentration of 0.25% DMSO. Competitive inhibition experiments are performed in triplicate in a final volume of 200 µL containing 4 pM [125I]ET-1 (1.6 nCi). Nonspecific binding is determined in the presence of 100 nM ET-1. Samples are incubated for 16 hours?18 hours at 24 °C. One milliliter of PBS is then added and the assay centrifuged at 2000 g for 25 minutes at 4 °C. The supernatant is decanted and the membrane bound radioactivity counted on a Genesys gamma counter.
Cell Research	TE 671 or transfected COS 7 cells are grown to confluence in six-well plates. Sixteen hours prior to use, the media in each well is replaced with 2 mL of inositol-free RPMI-164 (IF-RPMI) media containing 10% inositol-free FCS and 2 mCi [3H]myoinositol and incubated at 37 °C in the presence of 6% CO2. The media is aspirated, and the cells are washed twice with PBS. Cells are preincubated for 10 minutes in 1 mL of lithium buffer

	(15 μM HEPES, pH 7.4, 145 μM NaCl, 5.4 μM KCl, 1.8 μM CaCl2, 0.8 μM MgSO4, 1.0 μM NaH2PO4, 11.2 μM glucose, 20 μM LiCl) with or without Sitaxentan sodium prior to the addition of 100 μM of ET-1 at different concentrations. Cells are then incubated for an additional 45 minutes. The buffer is discarded, and the accumulated inositol phosphates are extracted with ice cold methanol. The total cell protein in each well is measured using the BCA assay after solubilizing the cells in 0.1 M NaOH.(Only for Reference)
Animal Research	Sitaxsentan is formulated in water.After an initial 2-week period of hypoxic exposure (10% O2) sitaxsentan (15 or 30 mg/kg body weight per day in the drinking water) is administered for 4 weeks during continuous exposure to hypoxia. At the conclusion of the 4 week period of hypoxia, femoral and pulmonary arterial cannulation and measurement of MPAP, MSAP, and HR are performed.

Solubility Information

Solubility	DMSO: 60 mg/mL (125.82 mM),Sonication is recommended. Ethanol: 20 mg/mL (41.94 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0969 mL	10.4846 mL	20.9692 mL
5 mM	0.4194 mL	2.0969 mL	4.1938 mL
10 mM	0.2097 mL	1.0485 mL	2.0969 mL
50 mM	0.0419 mL	0.2097 mL	0.4194 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Wu C, et al. J Med Chem. 1997, 40(11), 1690-1697.
Tilton RG, et al. Pulm Pharmacol Ther. 2000, 13(2), 87-97.
Wanebo JE, et al. Neurosurgery. 1998, 43(6), 1409-1417.
Holm P. Scand Cardiovasc J Suppl. 1997, 46, 1-40.