Tezosentan

Cat. No.: HY-17351

CAS No.: 180384-57-0

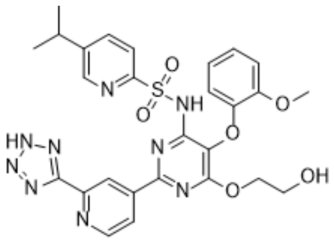
Molecular Formula: $C_{27}H_{27}N_9O_6S$

Molecular Weight: 605.63

Target: Endothelin Receptor

Pathway: GPCR/G Protein

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (82.56 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6512 mL	8.2559 mL	16.5117 mL
	5 mM	0.3302 mL	1.6512 mL	3.3023 mL
	10 mM	0.1651 mL	0.8256 mL	1.6512 mL

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

BIOLOGICAL ACTIVITY

Description

Tezosentan (RO 610612) is an endothelin (ET) receptor antagonist, with pA_2s of 9.5, 7.7 for ET_A and ET_B receptors, respectively.

IC_{50} & Target

ET_A	ET_B
9.5 (pA2)	7.7 (pA2)

In Vitro

Affinity of Tezosentan for the ET receptors is assessed in different cells and tissues. Tezosentan inhibits the specific ^{125}I-labeled ET-1 binding to ETA receptors with an inhibitory potency (K_i) of 0.3 nM on CHO cells and of 18 nM on membranes of baculovirus-infected insect cells. Similarly, Tezosentan inhibits the specific binding of ^{125}I-labeled ET-1, ET-3, or sarafotoxin S6c to ET_B receptors with an inhibitory affinity of 10 to 21 nM. Tezosentan up to a concentration of 1 μM did not exhibit any binding inhibitory activity in 27 radioligand binding assays different from ET binding. On H1 central, 5-hydroxytryptamine2A, and vasopressin V1 receptors, Tezosentan (1 μM) induces a weak inhibition of less than 20%[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

In pithed Wistar rats, Tezosentan dose-dependently inhibits the pressor effect of big ET-1 ($P<0.001$ at all doses). At the lowest dose tested of 1 mg/kg, Tezosentan inhibits the pressor effect of the various doses of big ET-1 by 50 to 80%.

Tezosentan has no effect by itself on blood pressure in these pithed rats. Tezosentan is very effective in a rat model of acute renal failure. ET antagonists have been shown to prevent the vasoconstriction and the renal failure that follow acute renal ischemia in rats[1].

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PROTOCOL

Animal Administration [1]

Rats[1]

A pseudocrush syndrome is simulated by injection of i.m. glycerol. A control group does not receive glycerol and is used as a reference. Tezosentan or bosentan for comparison or saline as control is injected as two bolus i.v. doses of 10 mg/kg 1 h and 20 min before glycerol. Rats are allowed to recover for 2 h and then are placed in individual metabolic cages for 48 h. Blood samples withdraw from a catheter placed in the abdominal aorta and urine free of food and feces are collected at 24 and 48 h. Plasma and urinary creatinine levels are measured with a centrifugal analyzer. Renal function is assessed by calculating creatinine clearance at 24 and 48 h after glycerol administration[1].

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

REFERENCES

[1]. Clozel M, et al. Pharmacology of tezosentan, new endothelin receptor antagonist designed for parenteral use. J Pharmacol Exp Ther. 1999 Aug;290(2):840-6.

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