Product Data Sheet

Product Name: Tezosentan (RO 610612)
Cat. No.: GC30942

Chemical Properties

Cas. No.	180384-57-0		
SMILES	O=S(C1=NC=C(C(C)C)C=C1)(NC2=NC(C3=CC(C4=NNN=N4)=NC=C3)=NC(OCCO)=C2OC5=CC=CC=C5OC)=O		
Formula	$C_{27}H_{27}N_9O_6S$	M.Wt	605.63
Solubility	DMSO : 50 mg/mL (82.56 mM; Need ultrasonic)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Tezosentan (RO 610612)		

Protocol

Animal experiment:

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].

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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.

Background

Tezosentan (RO 610612) is an endothelin (ET) receptor antagonist, with pA2s of 9.5, 7.7 for ETA and ETB receptors, respectively.

Affinity of Tezosentan for the ET receptors is assessed in different cells and tissues. Tezosentan inhibits the specific 125I-labeled ET-1 binding to ETA receptors with an inhibitory potency (Ki) 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 125I-labeled ET-1, ET-3, or sarafotoxin S6c to ETB 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].

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].

[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.

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