Darusentan

Cat. No.: HY-15404

CAS No.: 171714-84-4

Molecular Formula: $C_{22}H_{22}N_2O_6$

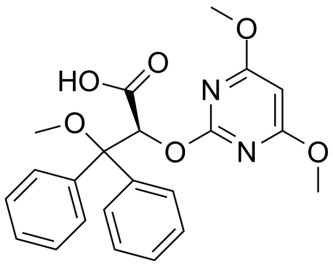
Molecular Weight: 410.42

Target: Endothelin Receptor

Pathway: GPCR/G Protein

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (243.65 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4365 mL	12.1826 mL	24.3653 mL
	5 mM	0.4873 mL	2.4365 mL	4.8731 mL
	10 mM	0.2437 mL	1.2183 mL	2.4365 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: ≥ 2.08 mg/mL (5.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Darusentan (Lu-135252) is a selective endothelin receptor A (ET-A) receptor antagonist, which binds with a K_i of 1.4 nM to the ET-A receptor and a K_i of 184 nM to ET-B receptor, respectively with a 100-fold selectivity for ETA rather than ETB receptors[1]. Darusentan competes for radiolabeled endothelin binding in rat aortic vascular smooth muscle cells (RAVSMs) membranes with single-site kinetics, exhibiting a K_i of 13 nM[2].

In Vitro

Darusentan ((S)-Darusentan) competes for radiolabeled endothelin binding in rat aortic vascular smooth muscle cells (RAVSMs) membranes with single-site kinetics, exhibiting a K_i=13 nM. In isolated endothelium-denuded rat aortic rings, Darusentan inhibits endothelin-induced vascular contractility with a pA_2=8.1±0.14. Darusentan (0.001-1μM) inhibits ET-1-induced signaling in cultured RAVSMs[2].

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

In Vivo

Darusentan (30 mg/kg per day orally for weeks 3 and 4) reverses aortic alterations produced by infusion of Norepinephrine (2.5 μg/kg per min subcutaneously for 2 and 4 weeks) in male Sprague Dawley rats[3].

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

Animal Model:	Twenty-four (eight per group) male Sprague Dawley rats weighing 175±200 g[3]
Dosage:	30 mg/kg
Administration:	Administered orally in rat food for weeks 3 and 4
Result:	Reversed aortic alterations produced by infusion of Norepinephrine (2.5 μg/kg).

REFERENCES

[1]. Liang F, et al. Darusentan is a potent inhibitor of endothelin signaling and function in both large and small arteries. Can J Physiol Pharmacol. 2010 Aug;88(8):840-9.

[2]. Frank Enseleit, et al. Darusentan, a selective endothelin A receptor antagonist, for the oral treatment of resistant hypertension. Ther Adv Cardiovasc Dis. 2010 Aug;4(4):231-40.

[3]. H H Dao, et al. Norepinephrine-induced aortic hyperplasia and extracellular matrix deposition are endothelin-dependent. J Hypertens. 2001 Nov;19(11):1965-73.

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