Bosentan (hydrate)

Cat. No.: HY-A0013A

CAS No.: 157212-55-0

Molecular Formula: $C_{27}H_{31}N_5O_7S$

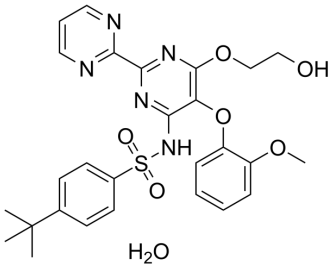
Molecular Weight: 569.63

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 (175.55 mM)

Ethanol : 50 mg/mL (87.78 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7555 mL	8.7776 mL	17.5553 mL
5 mM	0.3511 mL	1.7555 mL	3.5111 mL
10 mM	0.1756 mL	0.8778 mL	1.7555 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: ≥ 2.5 mg/mL (4.39 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.39 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.39 mM); Clear solution
4. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.39 mM); Clear solution
5. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Bosentan hydrate is a competitive and dual antagonist of endothelin-1 (ET) for the ET_A and ET_B receptors with K_i of 4.7 nM and 95 nM in human SMC, respectively.
IC_{50} & Target	Ki: 4.7 nM (ET_A receptor, in human SMC), 95 nM (ET_A receptor, in human SMC)[1]
In Vitro	Bosentan (BOS) competitively and specifically antagonizes binding of ^{125}I-labelled ET-1 to ET_A receptors on human smooth muscle cells (SMC) and ET_B receptors on human placenta cells. The in vitro binding affinity of Bosentan to ET_A receptors on human SMC is 4.7 nM and to ET_B receptors on human SMC or placenta cells is 41 or 95 nM. Bosentan has 67-fold greater selectivity for ET_A than ET_B receptors (mean IC_{50}=7.1 vs 474.8 nM) in an in vitro ^{125}I-labeling assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Single-dose Bosentan 62.5 mg significantly ($p<0.01$ vs baseline) plasma ET-1 levels by 2-fold in 7 pts with WHO class II or III idiopathic or CTD-associated PAH, with peak levels achieved at 8 h[1]. In hypertensive rats, Macitentan 30 mg/kg further decreases mean arterial blood pressure (MAP) by 19 mm Hg when given on top of Bosentan 100 mg/kg. Conversely, Bosentan given on top of Macitentan fails to induce an additional MAP decrease. In pulmonary hypertensive rats, Macitentan 30 mg/kg further decreases mean pulmonary artery pressure (MPAP) by 4 mm Hg on top of Bosentan, whereas a maximal effective dose of Bosentan given on top of Macitentan does not cause any additional MPAP decrease[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Cell viability is evaluated by the trypan blue exclusion test. Human dermal fibroblasts are treated with the indicated concentration of Bosentan (10, 20 and 40 μM). Cell viability is examined at 24 and 48 hours. Stained (dead) and unstained (viable) cells are counted with a hematocytometer[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Rats[3] Two-month-old DSS rats and two-month-old Wistar rats are used. Pharmacological effects on mean arterial pressure (MAP) or mean pulmonary arterial pressure (MPAP) and heart rate (HR) are measured up to 120 h after a single gavage at doses ranging from 0.1 to 100 mg/kg (Macitentan) or 3 to 600 mg/kg (Bosentan). To determine whether Macitentan can provide superior pharmacological activity vs. Bosentan, a study is designed in which: 1) Macitentan is administered on top of the maximal effective dose of Bosentan established by the dose-response curve. 2) the same dose of Bosentan is administered on top of the maximal effective dose of Macitentan. The maximal effective dose of the second compound is administered at T_{max} of the first tested compound. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Clin Immunol. 2023 Jul 5;109687.
- Hypertension. 2019 Dec;74(6):1409-1419.
- Acta Pharmacol Sin. 2022 Nov 30.
- Phytomedicine. 2023 Sep 2, 155054.
- Phytomedicine. 2019 Mar 15;56:175-182.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Dhillon S, et al. Bosentan: a review of its use in the management of mildly symptomatic pulmonary arterial hypertension. Am J Cardiovasc Drugs. 2009;9(5):331-50.

[2]. Akamata K, et al. Bosentan reverses the pro-fibrotic phenotype of systemic sclerosis dermal fibroblasts via increasing DNA binding ability of transcription factor Fli1. Arthritis Res Ther. 2014 Apr 3;16(2):R86.

[3]. Iglarz M, et al. Comparison of pharmacological activity of macitentan and bosentan in preclinical models of systemic and pulmonary hypertension. Life Sci. 2014 Nov 24;118(2):333-9.

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