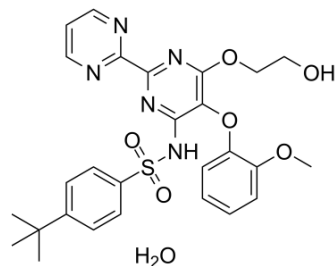


Bosentan (hydrate)

Cat. No.:	HY-A0013A		
CAS No.:	157212-55-0		
Molecular Formula:	C ₂₇ H ₃₁ N ₅ O ₇ S		
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	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (175.55 mM)
 Ethanol : 50 mg/mL (87.78 mM; Need ultrasonic)
 H₂O : < 0.1 mg/mL (insoluble)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

- 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
- 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
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (4.39 mM); Clear solution
- 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
- 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.
IC₅₀ & Target	Ki: 4.7 nM (ET _A receptor, in human SMC), 95 nM (ET _B 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 hemacytometer ^[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

- Hypertension. 2019 Dec;74(6):1409-1419.
- Cell Biol Toxicol. 2021 Jan 20.
- Phytomedicine. 2019 Mar 15;56:175-182.
- Toxicology. 2020 May 15;437:152445.
- Am J Physiol Heart Circ Physiol. 2019 Nov 1;317(5):H1166-H1172.

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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.

Caution: Product has not been fully validated for medical applications. For research use only.

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