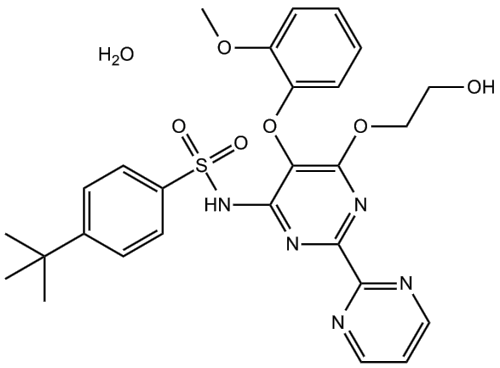
Product Data Sheet

Product Name: Bosentan Hydrate
Cat. No.: GC11465

Chemical Properties

Cas. No.	157212-55-0		
Chemical Name	4-tert-butyl-N-[6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2-pyrimidin-2-ylpyrimidin-4-yl]benzenesulfonamide;hydrate		
SMILES	CC(C)(C)C1=CC=C(C=C1)S(=O)(=O)NC2=C(C(=NC(=N2)C3=NC=CC=N3)OCCO)OC4=CC=CC=C4OC.O		
Formula	C27H31N5O7S	M.Wt	569.63
Solubility	≥ 28.5mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C 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



Protocol

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Cell experiment: 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].

Animal experiment: 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 Tmax of the first tested compound.

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.

Background

IC50: Inhibiting endothelin receptor A and B with an IC50 of 15.1 ± 1.6 μM in P388/dx cells.

A sulfonamide-derived, competitive and specific endothelin receptor antagonist with a relatively higher affinity to the endothelin A receptor than endothelin B receptor. By competitively binding to

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endothelin A and endothelin B receptors in the endothelium and vascular smooth muscle, Bosentan offset the effect of endothelin which is an extremely potent endogenous vasoconstrictor and broncho-constrictor. In addition, Bosentan decreases both pulmonary and systemic vascular resistance and is particularly applied in the treatment of pulmonary arterial hypertension. [1]

In vitro: A study was performed in vitro to measure the influence of Bosentan on the angiogenic performance of dermal microvascular endothelial cells (MVECs) and to detect the capacity of Bosentan in offsetting the antiangiogenic effects of systemic sclerosis sera. It was found that Bosentan significantly increased cell viability and offset the antiangiogenic effects of systemic sclerosis sera on dermal MVECs. [2]

In vivo: A study was conducted to investigate the effect of Bosentan on plasma leptin level after myocardial infarction in Wistar rats. After oral administration of Bosentan once daily at the dose of 100 mg/kg for 2 days, concentration of leptin in plasma significantly increased. This finding revealed that Bosentan played an crucial role on regulating leptin concentration in ischemic cardiovascular pathology. [1]

Clinical trials: A double-blind, placebo-controlled clinical trial was conducted to study the effect of bosentan on exercise capacity in a larger number of patients. 213 patients with pulmonary arterial hypertension were administered with 62.5 mg Bosentan twice daily for 4 weeks followed by either of two doses of Bosentan (125 or 250 mg twice daily) for a minimum of 12 weeks. It was found that 125 mg Bosentan was well tolerated and beneficial in patients with pulmonary arterial hypertension. [3]

References:
[1] Ostrowski RP, Januszewski SA, Kowalska ZA and Kapuscinski A. Effect of endothelin receptor antagonist bosentan on plasma leptin concentration in acute myocardial infarction in rats. Pathophysiology. 2003 Sep; 9(4): 249-56.
[2]Romano E, Bellando-Randone S, Manetti M, Bruni C, Lepri G, Matucci-Cerinic M, Guiducci S. Bosentan blocks the antiangiogenic effects of sera from systemic sclerosis patients: an in vitro study. Clin Exp Rheumatol. 2015 Aug; 33(4 Suppl 91): S148-52.
[3]Rubin LJ, Badesch DB, Barst RJ, Galiè N, Black CM et, al. Bosentan therapy for pulmonary arterial hypertension. New Engl J Med. 2002 Mar; 346 (12): 896-903.