Product Data Sheet

Product Name: A81988 (Abbott81988)
Cat. No.: GC32674

Chemical Properties

Cas. No.	141887-34-5		
SMILES	O=C(C1=CC=CN=C1N(CCC)CC2=CC=C(C3=CC=CC=C3C4=NNN=N4)C=C2)O		
Formula	$C_{23}H_{22}N_6O_2$	M.Wt	414.46
Solubility	Soluble in DMSO	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	A81988 (Abbott81988)		

Protocol

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Animal experiment:

Mice[2] B2-/- mice and wild-type J129Sv controls (B2+/+) are used. Pregnant mice are administered the nonpeptidic antagonist of Ang II AT1 receptors, A81988 (1.7 mg/kg BW per day in drinking water) or vehicle. At the dose indicated above, A81988 (A-81988) is able to antagonize the vasopressor effect of 10 pmol intravenous Ang II by 75% in mice. At 2 days after birth, the gender of the pups is determined, and each litter is culled to 5 male pups. Mice whose mother is treated during pregnancy continued to receive the antagonist until 180 days of age (treated B2+/+ and B2-/-, n=25 each group). Untreated controls of each strain (n=25 per group) are provided regular tap water. The animals are housed at a constant room temperature (24±1°C) and humidity (60±3%).Rats[3] Animals are randomly assigned to a normal (0.12 mmol/g chow, n=8 each group), a low (0.02 mmol/g chow, n=8 each group), or a high (0.84 mmol/g chow, n=8 each group) sodium diet. After 15 days, they received the antagonist A81988 (A-81988) for 10 days at the dose of 170 μg/100 g body wt per day orally. In the rat, the antagonist potency of A81988 on the vasopressor response to intravenous angiotensin II is greater than that of losartan by a factor of at least 10. A81988 has no affinity for adrenergic, cholinergic, endothelin, or PAF receptors, and it is >1000-fold more selective for AT1- versus AT2-receptors. In preliminary experiments, A81988 is able to antagonize the vasopressor effect of 10 pmol intravenous angiotensin II by 75%. Tail-cuff BP is measured twice under basal conditions, every 5 days during A81988 administration, and then after discontinuation of the compound.

References:

[1]. Hancock AA, et al. [3H]A-81988, a potent, selective, competitive antagonist

radioligand for angiotensin AT1 receptors. Eur J Pharmacol. 1994 Mar 15;267(1):49-54.
[2]. Madeddu P, et al. Angiotensin II type 1 receptor blockade prevents cardiac remodeling in bradykinin B(2) receptor knockout mice. Hypertension. 2000 Jan;35(1 Pt 2):391-6.
[3]. Madeddu P, et al. Circulation. 1997 Nov 18;96(10):3570-8.

Background

A81988 is a potent, competitive, non-peptidic antagonist of angiotensin AT1 receptors.

A81988 (A-81988) is labeled with tritium to high specific activity (16 Ci/mmol) and radioligand binding assays performed in rat liver membranes. [3H]A81988 binds with high affinity (KD=0.57 nM) and the KD determined from kinetics assays is similar. Non-specific binding (defined with 1 μM angiotensin-II) is very low (< 6% at the KD). The binding of

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[3H]A81988 is competitive and exhibits appropriate pharmacological specificity for compounds acting at angiotensin AT1 receptors[1].

To verify this hypothesis, B2-/- or wild-type mice (B2+/+) are administered a nonpeptide antagonist of Ang II type 1 (AT1) receptors (A81988) from conception through 180 days of age. Untreated B2+/+ and B2-/- served as controls. Blood pressure (BP) and heart rate are monitored with the use of tail-cuff plethysmography at regular intervals. Ventricular weights, diameters, wall thickness, chamber volume, and myocardial fibrosis are measured at 40 and 180 days. No differences are observed in BP, heart rate, and cardiac weight and dimensions between treated and untreated B2+/+. The BP of AT1 antagonist-treated B2-/- is reduced until 70 days; then, it increases to the levels found in untreated B2-/-. AT1 receptor blockade results in a reduction in left ventricular mass, chamber volume, and wall thickness and abrogated myocardial fibrosis in B2-/-[2]. A81988 (A-81988) decreases the BP of Bk2r-/- either in normosodic conditions or after sodium deprivation, whereas in Bk2r+/+ it produces a modest decrease under hyposodic conditions only[3].

[1]. Hancock AA, et al. [3H]A-81988, a potent, selective, competitive antagonist radioligand for angiotensin AT1 receptors. Eur J Pharmacol. 1994 Mar 15;267(1):49-54. [2]. Madeddu P, et al. Angiotensin II type 1 receptor blockade prevents cardiac remodeling in bradykinin B(2) receptor knockout mice. Hypertension. 2000 Jan;35(1 Pt 2):391-6. [3]. Madeddu P, et al. Circulation. 1997 Nov 18;96(10):3570-8.

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