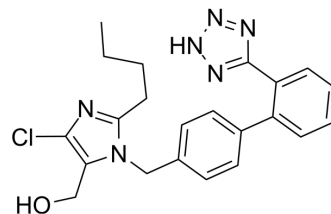


## Losartan

<b>Cat. No.:</b>	HY-17512		
<b>CAS No.:</b>	114798-26-4		
<b>Molecular Formula:</b>	C <sub>22</sub> H <sub>23</sub> ClN <sub>6</sub> O		
<b>Molecular Weight:</b>	422.91		
<b>Target:</b>	Angiotensin Receptor		
<b>Pathway:</b>	GPCR/G Protein		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	1 year
		-20°C	6 months



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 100 mg/mL (236.46 mM)  
 \* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.3646 mL	11.8228 mL	23.6457 mL
	5 mM	0.4729 mL	2.3646 mL	4.7291 mL
	10 mM	0.2365 mL	1.1823 mL	2.3646 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: ≥ 2.08 mg/mL (4.92 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
 Solubility: ≥ 2.08 mg/mL (4.92 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Losartan is an angiotensin II receptor antagonist, competing with the binding of angiotensin II to AT1 receptors with IC<sub>50</sub> of 20 nM.

#### IC<sub>50</sub> & Target

AT1 Receptor

#### In Vitro

Losartan competes with the binding of angiotensin II to AT1 receptors. The concentration that inhibits 50% of the binding of angiotensin II (IC<sub>50</sub>) is 20 nM<sup>[1]</sup>. Losartan (40 μM) affects I<sub>SC</sub> but prevents the effect of ANGII on I<sub>SC</sub><sup>[2]</sup>. Losartan significantly reduces Ang II-mediated cell proliferation in endometrial cancer cells. The combination of losartan and anti-miR-155 has a significantly greater antiproliferative effect compared to each drug alone<sup>[3]</sup>.

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

#### In Vivo

Losartan (0.6 g/L, p.o.) -treated Fbn1<sup>C1039G/+</sup> mice show a reduction in distal airspace caliber relative to placebo-treated Fbn1<sup>C1039G/+</sup> animals. The doses of losartan and propranolol are titrated to achieve comparable hemodynamic effects. Analysis of pSmad2 nuclear staining reveals that losartan antagonizes TGF- $\beta$  signaling in the aortic wall of Fbn1<sup>C1039G/+</sup> mice. Losartan can improve disease manifestations in the lungs, an event that cannot plausibly relate to improved hemodynamics<sup>[4]</sup>. Losartan (10 mg/kg, intraarterial injection) increases blood angiotensin levels four- to sixfold. Losartan (10 mg/kg, i.p.) increases plasma renin levels 100-fold; plasma angiotensinogen levels decreases to 24% of control; and plasma aldosterone levels are unchanged<sup>[5]</sup>.

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## PROTOCOL

#### Cell Assay <sup>[3]</sup>

An MTT assay is used to measure cell proliferation and viability. For the assay, 5000 cells in 200  $\mu$ L media per well are seeded in a 96 well plate. After overnight incubation to allow for cell attachment, the medium is removed by suction. MTT at 1 mg/mL concentration in serum-free medium is added and then incubated for 4 h at 37°C. After removal of MTT solution, 100  $\mu$ L of DMSO is added to dissolve formazan crystals. Absorbance at 570 nm and at 600 nm as a reference is then measured using a microplate reader. The difference in absorbance is thus relative to the extent of cell survival.

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#### Animal Administration <sup>[4]</sup>

Female Fbn1<sup>C1039G/+</sup> mice undergo timed matings with wild-type male mice. At 14.5d post-coitum, pregnant female Fbn1<sup>C1039G/+</sup> mice are treated with oral losartan (0.6 g/L in drinking water; n=10), propranolol (0.5 g/L; n=6) or placebo (n=12). Therapy is continued throughout lactation and after weaning until 10 months of age. Mice are sacrificed and examined using the techniques described above. Propranolol is used for comparison with losartan because  $\beta$ -adrenergic receptor blockade is the current albeit controversial standard of care to modulate abnormal growth of the aortic root in MFS. Beginning at 7 weeks of age, wild-type and Fbn1<sup>C1039G/+</sup> mice are treated with oral losartan (0.6 g/L in drinking water; n=5), propranolol (0.5 g/L; n=7) or placebo (n=10). Mice are continued on oral therapy for 6 months and then sacrificed.

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

## CUSTOMER VALIDATION

- Clin Transl Med. 2023 Mar;13(3):e1213.
- Cell Death Dis. 2020 May 22;11(5):390.
- Oncogene. 2023 Feb 23.
- Int J Nanomedicine. 2018 Nov 13;13:7409-7426.
- Phytomedicine. 2023 Feb 4;112:154700.

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## REFERENCES

- [1]. Burnier, M. Angiotensin II type 1 receptor blockers. *Circulation*, 2001. 103(6): p. 904-12.
- [2]. Ashry, O., et al. Evidence for expression and function of angiotensin II receptor type 1 in pulmonary epithelial cells. *Respir Physiol Neurobiol*, 2014.
- [3]. Choi, C.H., et al. Angiotensin II type I receptor and miR-155 in endometrial cancers: synergistic antiproliferative effects of anti-miR-155 and losartan on endometrial cancer cells. *Gynecol Oncol*, 2012. 126(1): p. 124-31.

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[4]. Habashi, J.P., et al. Losartan, an AT1 antagonist, prevents aortic aneurysm in a mouse model of Marfan syndrome. *Science*, 2006. 312(5770): p. 117-21.

[5]. Campbell, D.J., et al. Effects of losartan on angiotensin and bradykinin peptides and angiotensin-converting enzyme. *J Cardiovasc Pharmacol*, 1995. 26(2): p. 233-40.

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

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