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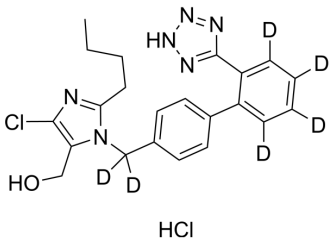
Losartan-d_6 hydrochloride

Cat. No.:	HY-17512AS
Molecular Formula:	$C_{22}H_{18}D_6Cl_2N_6O$
Molecular Weight:	465.41
Target:	Angiotensin Receptor; Isotope-Labeled Compounds
Pathway:	GPCR/G Protein; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Losartan-d_6 hydrochloride is deuterated labeled Losartan potassium (HY-17512A). Losartan potassium (DuP-753 potassium) is an angiotensin II receptor type 1 (AT1) antagonist, competing with the binding of angiotensin II to AT1 with an IC_{50} of 20 nM.
In Vitro	Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1]. Losartan competes with the binding of angiotensin II to AT1 receptors. The concentration that inhibits 50% of the binding of angiotensin II (IC_{50}) is 20 nM[2]. Losartan (40 μM) affects I_{SC} but prevents the effect of ANGII on I_{SC}[3]. 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[4]. 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 $Fbn1^{C1039G/+}$ mice show a reduction in distal airspace caliber relative to placebo-treated $Fbn1^{C1039G/+}$ animals. The doses of losartan and propranolol are titrated to achieve comparable hemodynamic effects. Analysis of pSmad2 nuclear staining reveals that losartan antagonizes TGF-β signaling in the aortic wall of $Fbn1^{C1039G/+}$ mice. Losartan can improve disease manifestations in the lungs, an event that cannot plausibly relate to improved hemodynamics[5]. 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[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Burnier, M. Angiotensin II type 1 receptor blockers. Circulation, 2001. 103(6): p. 904-12.

[2]. 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]. Ashry, O., et al. Evidence for expression and function of angiotensin II receptor type 1 in pulmonary epithelial cells. Respir Physiol Neurobiol, 2014.

[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.

[6]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. Ann Pharmacother. 2019 Feb;53(2):211-216.

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