Losartan Carboxylic Acid

Cat. No.: HY-12765

CAS No.: 124750-92-1

Molecular Formula: $C_{22}H_{21}ClN_6O_2$

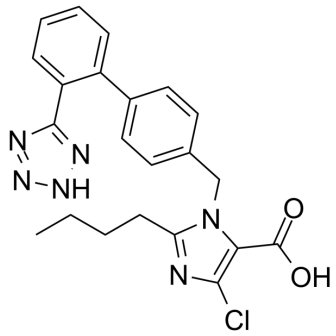
Molecular Weight: 436.89

Target: Angiotensin Receptor

Pathway: GPCR/G Protein

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 250 mg/mL (572.23 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2889 mL	11.4445 mL	22.8891 mL
	5 mM	0.4578 mL	2.2889 mL	4.5778 mL
	10 mM	0.2289 mL	1.1445 mL	2.2889 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.76 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.76 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Losartan Carboxylic Acid (E-3174), an active carboxylic acid metabolite of Losartan, is an angiotensin II receptor type 1 (AT1) antagonist. The K_i values are 0.97, 0.57, 0.67 nM for rat AT1B/AT1A and human AT1, respectively. Losartan Carboxylic Acid blocks the angiotensin II-induced responses in vascular smoothmuscle cells (VSMC). Losartan Carboxylic Acid elevates plasma renin activities and reduces mean arterial pressure[1][2][3][4].

IC_{50} & Target

Angiotensin II receptor type 1[1]

In Vitro

The specific binding of [125I]-angiotensin II to VSMC is inhibited by Losartan Carboxylic Acid (E-3174) with an IC_{50} of 1.1 nM. Losartan Carboxylic Acid abolishes the angiotensin II-induced formation of inositolphosphates in VSMC. Losartan Carboxylic

Acid inhibits the angiotensin II-induced elevation of intracellular cytosolic Ca2+ concentration with an IC_{50} of 5 nM. Losartan Carboxylic Acid is more effective than losartan in blocking the angiotensin II-induced increase in Egr-1 mRNA. Losartan Carboxylic Acid inhibits the angiotensin II-induced cell protein synthesis with an IC_{50} of 3 nM[1].

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

In Vivo

Losartan Carboxylic Acid (E-3174) (0.1 mg/kg; i.v. followed by 0.02 mg/kg/h for 5.5 h) induces a similar level of inhibition (87±4%) of the pressor responses to angiotensin I[3].

Intravenous Losartan Carboxylic Acid (0.1 mg/kg+0.01 mg/kg/min) is infused in anesthetized dogs with recent (8.1±0.4 days) anterior myocardial infarction. Electrolytic injury of the left circumflex coronary artery to induce thrombotic occlusion and posterolateral ischemia is initiated 1 h after the start of treatment[4].

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

Animal Model:	Mongrel dogs of either sex, weighing 15-25 kg[3]
Dosage:	0.1 mg/kg (followed by 0.02 mg/kg/h)
Administration:	i.v. for 5.5 hours
Result:	The pressor response was reduced by 87±4%.

REFERENCES

[1]. Sachinidis A, et al. EXP3174, a metabolite of losartan (MK 954, DuP 753) is more potent than losartan in blockingthe angiotensin II-induced responses in vascular smooth muscle cells. J Hypertens. 1993 Feb;11(2):155-62.

[2]. Inada Y, et al. Binding of KRH-594, an antagonist of the angiotensin II type 1 receptor, to cloned human and rat angiotensin II receptors. Fundam Clin Pharmacol. 2002 Aug;16(4):317-23.

[3]. Richard V, et al. Comparison of the effects of EXP3174, an angiotensin II antagonist and enalaprilat on myocardial infarct size in anaesthetized dogs. Br J Pharmacol. 1993 Nov;110(3):969-74.

[4]. Lynch JJ Jr, et al. EXP3174, the AII antagonist human metabolite of losartan, but not losartan nor the angiotensin-converting enzyme inhibitor captopril, prevents the development of lethal ischemic ventricular arrhythmias in a canine model of recent myoca

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